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SOME PHILOSOPHICAL ASPECTS OF THE PROBLEM OF 'MAN, THE BIOSPHERE AND SPACE'

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 6, 1979 pp 1-9

[Article by N. A. Agadzhanyan, submitted 15 Jun 77]

[English abstract from source]

The paper discusses philosophic approaches to the problem of man-environment interplay. Many important problems humanity faces today are associated with biology. Biomedical and astrophysical studies are being carried out to gain a better insight into the laws governing evolution and further development of the Universe. The emergence of a human society started a qualitatively new stage in the evolution of organic matter. A rapid progress of science and engineering is accompanied by a significant rearrangement of the natural environment and, particularly, of living beings. The biosphere is transforming into the sphere of intelligence, i. e. noosphere. However, natural phenomena are still more powerful than man-made productive forces.

Man's excursion into outer space allowed him to look at himself as if from the outside and to evaluate critically his actual role, position and responsibility in the infinite Universe as compared with other forms of life and intelligence. The Universe may be boundlessly great but for human beings there is nothing better than the Earth. Our planet will long remain the base for the existence and development of humanity. Today man ought to take the streering-wheel of evolution and fate of the biosphere into his hands, in order to preserve, through the efforts of many generations, our planet as the gem of the Universe.

[text] The entire history of mankind, from the Stone and Bronze ages to the atomic and space age, is characterized by the continuous development of society. There is an ascending and a descending branch in each history, and the history of mankind is hardly an exception. Unquestionably, the 20th century is the most revolutionary one in the entire history of mankind. Virtually within the lifetime of a single generation, comfortable motor vehicles and supersonic aircraft, radio communications and multichannel radio receivers, motion pictures and television, electronic computers and spacecraft have appeared. The striking advances made in different branches of science have led to unprecedented,profound and basic economic and social changes in the life of man, and they have significantly broadened our perception and awareness.of the world.

It was noted at the 25th CPSU Congress that "the deep stream of scientific and technological progress would run dry if it were not constantly nurtured by basic research." In the opinion of many scientists, biology, cybernetics, gene engineering, oceanology, thermonuclear energy and astrophysics will be the main branches of science at the end of the second and beginning of the third millenium. Astrophysical and biomedical research will direct itself toward learning the laws of the universe, its evolution and ultimate fate.

As we solve the many pressing problems that confront mankind today, we usually find that the roots of most of them go back to biology. When scrutinizing questions of population growth on earth and the prospects of providing people with food and water, protection of the atmosphere and earth from pollution by industrial waste and control of diseases, increase in energy consumption and prospects of development of aviation and cosmonautics, we become convinced each time that our knowledge is inadequate in the area of the main phenomena of living matter, in biology. This is attributable to the complexity of the object of investigation.

In the history of our planet, from the day it was formed and to the present time, awe-inspiring processes are continuously taking place on a planetary scale, which transform radically the image of earth. The appearance and development of an ecological system and life on earth is the result of a lengthy, diversified and nonuniform process of evolution of matter, the essence of which consists of refinement and progressive differentiation of forms of movement thereof. In turn, differentiation was based on progressive integration of more and more new structural elements.

In the currently prevailing theories of evolution, which are based on the conception of development from the simple to the complex, more and more argumented contradictions are accumulating. At the same time, a basically new approach is forming, which develops the ideas of V. I. Vernadskiy to the effect that life appeared on earth and evolved as a single planetary system, the biosphere [1].

As far back as 1926, in the foreword to "Biosfera" [The Biosphere], V. I. Vernadskiy wrote, in backing up the idea that life is a cosmic phenomenon rather than a specially terrestrial one: "Life is viewed as a chance phenomenon on earth, for which reason the influence of the living on the course of terrestrial processes that is manifested at each step disappears from our scientific horizon: life did not develop by chance nor did the biosphere, this special life-containing envelope, on the surface of the planet, on the boundary with the cosmic environment" [2]. He stressed that one should not search for evidence of the start of life on our planet or planets in general, but for the physical and energy conditions of manifestation of planetary life.

With the appearance of a human society, a basically new stage began in evolution of the organic world. By virtue of the global nature of interaction with the environment, man became, for the first time, the strongest geological force.

Intensive scientific and technological progress is associated with a substantial change in the environment, and particularly its living surface. The biosphere is literally being transformed into a world of intelligence, a noosphere. This fact per se is a natural process, but the future of our planet depends largely on whether man's conscious endeavors will be directed toward creation and wise use of natural resources.

There are figures and facts that eloquently describe the intensive pace of the scientific and technological revolution. Zh. Pla writes: "In the last 100 years we have increased by 10,000,000 times the speed of our communications, by 100 times the speed of our travel, by 1000 times our energy resrouces and by 1,000,000 times the capability of our weapons" [3].

Man's industrial endeavors are related not only to the production of the necessities of life [material wealth], but pollution of the environment by industrial waste. Yes, modern man is altering the structure of earth's crust, increasing biogenous migration of atoms, developing new forms of plants and animals, augmenting their producitvity, and acclimating to new habitats. But, unfortunately, intervention in nature often brings great harm, along with benefits.

The productive forces of our environment are still stronger than the productive forces created by man. The biosphere of our planet performs geochemical and energetic work, which exceeds substantially in its scale the capabilities of modern worldwide industry. But the power of man, armed with the latest scientific advances, is already becoming commensurate with that of nature, and if man is only concerned with current problems he is capable, in principle of seriously disrupting the balance of nature over wide areas and thereby cause irreparable harm to the natural resources and biosphere of our planet. For expressly this reason the natural sciences, which deal with nature, play such a large role in contemporary development of society. For expressly this reason, the problems of "man and the biosphere" and "man, society and the environment" have become the "topic of the century." They are no the primary concern of the worldwide community, and they are becoming the subject of scientific research on a worldwide scale.

In the Soviet Union, concern about the environment ranks high as a problem. From the very first day after the Great October Socialist Revolution, V. I. Lenin prepared the text for a decree pertaining to the land, proclaiming that all of the natural resources are public property. This eliminated the main cause of plundering of natural resources, the despotism of private owners.

Since it is easier to organize the use of natural resources than protection and reproduction thereof, V. I. Lenin devoted much attention to problems of environmental protection, adding them to objectives of scientific research as the mandatory basis for any socially useful activity. He repeatedly stressed that the success of any state or political work depends significantly on acquiring and using special scientific knowledge. In a report on the Party program at the 8th Party Congress, V. I. Lenin indicated that research must be pursued without regretting the expenses for science: "This will be the best policy, this will be the most economical management. Otherwise, by saving a few hundred millions, we shall lose so much that no billions would restore what is lost" [4].

The ideas of V. I. Lenin about environmental protection and wise use of natural resources were embodied in the socialist principles of policy in the use of natural resources.

The distinctive feature of the modern era is that now, as never before, we find a need, not only of society but of each individual on this planet, for the entire diversity of its resources transformed by the many centuries of man's labor. This is what P. Teilhard de Chardin writes on this score in his book "The Phenomenon of Man" (1965): "At the present time, each man needs his daily portion of iron, copper and cotton, his portion of electricity, oil and radium, his portion of discoveries, movies and international news, in addition to bread, which symoblized in its simplicity the food of the Neolithic period. At present, it is not a simple field, no matter how large, but all of earth that is needed to provide for each of us" [5]. Finally, in order to use the resources of our planet, we must realize that not only does each of us need earth, but that earth needs each of us. Earth, in the literal sense of the word, is becoming a planet for people, the planet of Mankind.

Through all of the historical eras, a typical distinction of development of intelligent life was its constant tendency toward unlimited expansion, toward broadening the sphere of its activity. Without this, the development of any civilization is inconceivable.

The calendar for the second half of the 20th century already contains many noteworthy dates of the space age. And we, the Soviet people, are entitled to be proud of the fact that this age [era] began in our country, the world's first socialist state. Only 20 years ago, on 4 October 1957, the world's first artificial satellite of earth was launched in the USSR. The first satellite was followed by others, making true the age-old dream of mankind: to penetrate deep into the universe. On 12 April 1961, Yu. A. Gagarin was the first man to see the majestic view of the universe and our beautiful planet through the window of the Vostok-1 spacecraft. Man's penetration into space is, unquestionably, one of the most noteworthy and exciting milestones in the history of mankind. The Soviet cosmonaut, Yu. A. Gagarin, with his first space flight, shattered, so to speak, once and for all, the myth conceived in ancient times about Icarus, who tried to fly toward the sun wearing wings of feathers, joined with wax. Also irretrievably gone is the myth about the infiniteness of earth. Marx wrote: "All of mythology overcomes, subordinates and transforms the forces of nature in the imagination and by means of imagination; consequently, it disappears with the appearance of real dominion over these forces of nature" [6]. Man's attitude toward heaven, the planets and stars of the universe, always had philosophical importance. In our space age, time is running quite fast. It would seem that the space age has only begun. Yet, the first artificial satellite of earth was followed by the first manned space flight, extravehicular activity, docking of spacecraft and creation of orbital stations. Earthlings have been on the moon; sensitive machines have worked on the moon, Venus and Mars; photos have already been taken even of Mercury and Jupiter, and an emissary from earth is flying to Uranus.

Development of cosmonautics has a considerable influence, not only on overall scientific and technological progress, but all aspects of life of modern man. The information obtained as a result of space research has enriched the basic sciences to an exceptional extent, it has broadened the sphere of our perception of the world and thinking, it has aided in broader philosophical interpretation of environmental phenomena, and it has affected development of our conceptions of the universe.

The practical demands for conquering space not only make it necessary to gain comprehensive knowledge about the properties of space objects, distinctions of closest planets and space, but compel us to refer to philosophical premises [or prerequisites] and methodological aspects of studying life in space, since it is expressly the solution of philosophical problems that provides an integral idea about man's attitude [relation] toward the world.

Man's excursion into space enabled him to take a look at himself for the first time from the outside, so to speak, and from this new position to make a certain critical self-appraisal of the real role, responsibility and place of mankind in the infinite universe around us, among other forms of life and intelligence.

Availability of energy is of first and foremost importance to the development of the material base of society and stimulation of scientific research. The intensive development of the national economy and rapid growth of the population of earth cause continuous increase in recovery of fuel. It is doubling approximately every 20 years. In this connection, a cardinal question has arisen: how long will the supply of combustible minerals last? It has been estimated that, even if future geological exploration and improvement of the recovery coefficient lead to an increase in reserves, let us say, by 8 times, the supply of fuel would be exhausted sometime in 2110. This is not a long term at all. For expressly this reason the scientists are trying the forecast, on the solid foundation of basic scientific knowledge, the state of society, its economy and material and technical base in the foreseeable future, and first of all they are searching for a solution to the main problem, that of creating a basically new base for worldwide energy.

People of the future, knowing the present and future, will obtain energy more from space than the bowels of the earth. Solar energy is the most important resource of the universe. Indeed, earth receives from the sun as much energy in 10 days as could be obtained by burning all the supplies of organic fuel. It is expressly the development of solar energy that K. E. Tsiolkovskiy viewed as the loftiest objective of cosmonautics. In his works, he also posed several important sociological questions of space exploration. He expounded his philosophical and sociological ideas considerably earlier than those pertaining to rocket theory.

As far back as 1923, K. E. Tsiolkovskiy tried to single out not only the main directions of interaction between society and the environment, but the significance of the main basic sciences in this process, in particular biology. "Biology," he wrote, "will serve to transform plants and to improve the human race. Socialistic sciences will make it possible to extract the very best from mankind and thereby accelerate achievement of all possible good accessible to man" [7]. Through his works, K. E. Tsiolkovskiy widened the range of human cognition and perception, he cooperated with propaganda and natural scientific substantiation and development of materialism.

While he was not a philosopher by education, he expounded an orderly system of views on the cosmic future of mankind, which was profoundly materialistic. It is based on the thesis that the human race will never perish. "I believe in the brilliant future of mankind, I believe that mankind will not only inherit the earth, but will transform the world of planets. Man will migrate from here, from the spehre of the sun, and he will begin to settle all over the universe. I am firmly convinced of this. This is the destiny of terrestrial man. He must transform many planetary systems" [8].

He wrote with inspiration and conviction about the advantages of life in cosmic space. But this dreamer-scientist never called upon all of mankind to leave earth for the heavens; this was merely a way out in the event of some cosmic catastrophe, a way out that is dictated by faith in the infinite progress of the human race. He called upon exploration of the space near the sun expressly in the interests of earth.

If the resources of large planets are used, the surface of the artificial biosphere in the solar system could be hundreds of thousands of times larger than the surface of our globe. This will involve interception and transformation of solar energy constituting hundreds of billions of times more than the present use of energy on earth. What is the time scale for such development? In order to erect space colonies with a population of 10 billion, about 250 years will be required according to the estimates. With such exponential growth, it will take about 500 years to develop [conquer] all of the physical resources of the solar system.

As he developed the scientifically substantiated principles of development and settlement of cosmic space by mankind, K. E. Tsiolkovskiy repeatedly stressed that our planet will remain as the basis for the existence of mankind for a long time yet. "Earth," he wrote, "is needed as a support, as the basis for dissemination and consolidation of man's power in the solar system and on its planets."

The question of interaction between man and the environment in our powerful 20th century is not only a technical, economic, political and social question; it is also a moral and ethical one, a purely human one, since "... the essence of man is not an abstraction inherent in a single individual. In reality, it is the aggregate of all social relations" [9]. In turn, with development of the biosphere and society, there should also be development of each individual person.

Scientific and technological progress, which is determined by the objective laws of development of society, is inevitable. What is the alternative?

Replacement of the biosphere with a technosphere, or migration to other planets and conquest of all the space around the sun? All this is tempting. But will people who suddenly find themselves incapable of existing on their own planet be able to develop world space? If it will be so inevitable to fly into space, one should take along not only a "little piece" of our beautiful earth, but our beautiful souls and thoughts. For the sake of this noble goal and future purposeful and progressive development, mankind must take the helm of evolution and the fate of the biosphere in his hands right now.

We are making a close study and analysis of information about future technological progress and resources of the earth, structure and physicochemical properties of planets, galactic phenomena and the stormy life of the universe, but at times we forget that man, as an object of nature, has more complex internal and external interactions, and he requires more comprehensive study than the entire galactic system. We forget the fact that, in the presence of such a disproportion, we inexcusably rob ourselves for the sake of technological progress and we occasionally achieve the latter to the detriment of spiritual and biological progress.

Social, scientific and technological progress has gained an intensive momentum on the threshold of the new, third, millenium. All this is gradually leading to change in man's life style and in his biological and social interaction with all of his environment. Witnessing the scientific and technological revolution, we very often fail to notice and realize that we are also becoming the contemporaries of the scientific and technological revolution, a new revolution of the biosphere.

One must also bear in mind that man is a social being. The biological element does not dominate in man and should not rule over him.

In solving the most basic biomedical problems, it is also inadmissible for us to overlook the legal, ethical and esthetic aspect of interpersonal relations. Some remedies, even if they do improve the biological nature of man, could lead to his social degradation.

No matter how large the world may be, there is nothing better for man than earth. The planet earth is still our only home, where we toil and live. And even though there are planets suitable for life in our Galaxy, for a long time yet mankind will live on earth's surface. Profusely covered with sweat and blood, our native planet will be preserved as the pearl of cosmos through the efforts of future generations.

In the message of our Party and government congratulating all those who participated in the world's first successful manned space flight, it was stated: "Our free, talented and industrious people, inspired ["uplifted"] for conscious historical creativity in October 1917 by the party of communists, headed by the great leader and teacher of workers of the world, Vladimir Il'ich Lenin, is showing the entire world the supreme advantages of the new socialist regime to all areas of life of society."

Each step toward conquering space is a stellar salute to the Great October Revolution.

BIBLIOGRAPHY

1. Verdandskiy, V. I. "Thoughts of a Naturalist," Moscow, Bk 1, 1975; Bk 2, 1977.
2. Idem "The Biosphere," Leningrad, 1926.
3. Agadzhanyan, N. A. "The Kernel of Life," Moscow, 1977, p 6.
4. Lenin, V. I. "Poln. sobr. soch." [Complete Collection of Works], Vol 38, p 168.
5. Teilhard de Chardin, P. "The Human Phenomenon," Moscow, 1965, p 241.
6. Marx, K., and Engels, F. "Works," 2d edition, Vol 46, Pt 1, p 47.
7. Tsiolkovskiy, K. E. "Sobr. Soch." [Collected Works], Moscow, Vol 4, 1954, p 296.
8. Quoted by Lyapunov, B. and Nikolayev, N. "Through the Thorns to the Stars," Moscow, 1962, p 167.
9. Marx, K., and Engels, F. "Works," 2d edition, Vol 3, p 3.

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COMPOSITION OF INTESTINAL MICROFLORA OF COSMONAUTS BEFORE AND AFTER SPACE FLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 6, 1979 pp 9-13

[Article by N. N. Liz'ko, V. M. Shilov, G. D. Syrykh and V. I. Legen'kov, submitted 15 May 78]

[English abstract from source]

The composition of the intestinal microflora of 12 cosmonauts was studied before and after space missions of varying duration. Changes in the intestinal microbial coenosis were found prelaunch. The pattern of changes did not vary with an increase in space flight duration. The use of special prophylactic measures exerted a positive effect on intestinal microecology. Bifidobacteria and lactobacilli showed the greatest changes inflight. Therefore, it seems important to arrange preflight sanation of the intestinal microflora as a prophylactic method.

[Text] Numerous studies in the form of ground-based model experiments established that exposure to extreme factors during space flights leads to significant changes in composition of intestinal microflora [1-3].

It has been shown in works by Soviet and American authors that impairment of composition of microflora could have an adverse effect on health and fitness of cosmonauts during space flights [4-7].

For this reason, it was interesting to demonstrate the distinctions of microbiocenosis of the intestine of cosmonauts involved in orbital space flights varying in duration, in the preflight and postflight periods.

In this work, we submit the results of studies of quantitative and qualitative composition of intestinal microflora of 12 cosmonauts, before and after 2-, 5-, 7- and 8-day orbital flights aboard the Soyuz-12, Soyuz-13, Soyuz-16 and Soyuz-19 spacecraft, as well as 30- and 63-day missions aboard the Salyut-4 orbital station.

Methods

The intestinal microflora was examined at the following times: preflight period (20 days before flight), prelaunch period (1-3 days before lift-off), postflight period (1st day), as well as later times following long-term flights.

The quantitative composition of fecal microflora was examined by the method of Haenel as modified by N. N. Liz'ko [8]. The following groups of microorganisms were studied: total number of aerobic bacteria, staphylococcus, streptococcus, proteus, E. coli, lactobacillus, bacteroids, bifidobacteria, anaerobic bacteria, sporulated anaerobic bacilli and yeast. The overall amount of anaerobic bacteria, bacteroids, bifidobacteria and lactobacilli was determined by superposing hour glasses with 4-6-h culture of Serratia marcescens on dishes with nutrient medium to create anaerobic conditions.

For this purpose, we applied 1-2 mℓ nutrient agar (depending on the depth of the glasses) on watch glasses, dried it for 20 min at 37°C temperature and then added the suspension of Serratia marcescens culture, which was prepared with washings from a day-old culture from slant agar with 10 mℓ sterile water. The suspension prepared in this manner covered the surface of agar decanted on the watch glasses and the treated watch glasses were held in an incubator for 4-6 h. After this, watch glasses, under which anaerobic conditions were created for culturing the above groups of microorganisms, were applied over the site of application of drops of the appropriate dilutions of feces on selective nutrient media.

Results and Discussion

The data obtained from our study of quantitative composition of intestinal microflora of the cosmonauts are indicative of appearance of marked changes in microbial cenosis of the intestine in the prelift-off period. Thus, V. G. Lazarev (Table 1) present a significant (100-fold) decrease in lactobacillus content, and O. G. Makarov presented a drastic decrease in number of these bacteria (1000-fold) and a decrease in bifidobacteria (100-fold). After the flight, the lactobacillus content reached the background level in the former, while both lactobacillus and bifidobacteria content of the latter remained the same as in the prelaunching period.

More marked changes in aerobic microflora were observed in the prelaunch period in A. V. Filipchenko and N. N. Rukavishnikov (Table 2). Thus, there was significant increase in E. coli content (by more than 100 times) in the spacecraft commander, an increase in proteus content and tendency toward decrease in bifidobacteria in A. V. Filipchenko, with increase in streptococcus (by about 100 times) in both cosmonauts.

In the postflight period, along with restoration of aerobic flora, we observed a drastic decrease (1000-fold) in lactobacillus content in both cosmonauts, and a significant increase in sporulated anaerobic bacteria (1000-fold) in N. N. Rukavishnikov.

The intestinal microflora was characterized by a change in bifidoflora in the prelaunch period in cosmonaut crew members of Soyuz-19 (see Table 1). Thus, A. A. Leonov presented a decrease (by more than 100 times) in bifidobacteria, while this group of microorganisms was not demonstrable in V. N. Kubasov at the same examination time.

Table 1. Changes in bifidobacteria and lactobacillus content in the crews of Soyuz-12 and Soyuz-19 spacecraft

Cosmonaut	Bifidobacteria			Lactobacilli		
	Day of examination					
	preflight		postflight	preflight		postflight
	20th	1st-3d	1st	20th	1st-3d	1st
V. G. Lazarev	$8{,}0\cdot10^{7}$	$5{,}9\cdot10^{8}$	$3{,}2\cdot10^{8}$	$1{,}0\cdot10^{8}$	$1{,}0\cdot10^{4}$	$1{,}0\cdot10^{7}$
O. G. Makarov	$2{,}4\cdot10^{7}$	$8{,}0\cdot10^{6}$	$8{,}0\cdot10^{6}$	$1{,}0\cdot10^{8}$	$1{,}0\cdot10^{3}$	$1{,}0\cdot10^{8}$
A. A. Leonov	$1{,}0\cdot10^{8}$	$3{,}0\cdot10^{8}$	$2{,}0\cdot10^{7}$	$8{,}0\cdot10^{6}$	$3{,}2\cdot10^{7}$	$1{,}8\cdot10^{7}$
V. N. Kubasov	$2{,}0\cdot10^{7}$	None found	$7{,}0\cdot10^{8}$	$3{,}4\cdot10^{7}$	$1{,}0\cdot10^{8}$	$1{,}2\cdot10^{7}$

Note: Quantitative data are given only for the groups of microorganisms in which changes were noted.

Table 2. Changes in quantitative composition of different representatives of intestinal microflora in the crew of Soyuz-16 spacecraft

Group of microorganisms	A.V. Filipchenko			N. N. Rukavishnikov		
	day of examination					
	preflight		postflight	preflight		postflight
	20th	1st-3d	1st	20th	1st-3d	1st
Streptococcus	$2{,}0\cdot10^{4}$	$3{,}6\cdot10^{6}$	$4{,}0\cdot10^{5}$	$2{,}0\cdot10^{4}$	$1{,}0\cdot10^{6}$	$2{,}0\cdot10^{4}$
Proteus	$1{,}0\cdot10^{3}$	$1{,}0\cdot10^{4}$	$1{,}0\cdot10^{3}$	$1{,}0\cdot10^{3}$	$1{,}0\cdot10^{4}$	$1{,}0\cdot10^{2}$
E. coli	$6{,}0\cdot10^{5}$	$6{,}4\cdot10^{7}$	$1{,}4\cdot10^{7}$	$8{,}0\cdot10^{7}$	$9{,}0\cdot10^{7}$	$2{,}0\cdot10^{8}$
Lactobacilli	$2{,}0\cdot10^{6}$	$3{,}6\cdot10^{7}$	$2{,}0\cdot10^{4}$	$5{,}8\cdot10^{7}$	$9{,}2\cdot10$[illegible]	$3{,}0\cdot10^{6}$
Spore-bearing anaerobic bacilli	None found	None found	None found	$9{,}0\cdot10^{2}$	$5{,}0\cdot10^{2}$	$2{,}0\cdot10^{8}$

Some restoration of bifidoflora was noted in the postflight period, but it did not reach the background level.

Analogous changes in microbial cenosis of the intestine were demonstrated in the prelaunch period in the crew of Soyuz-13, and they were characterized by a decrease in bifidobacterium content in O. I. Klimuk, and increase in aerobic microorganisms in both cosmonauts (Table 3). The most marked change was the increase in streptococcus content in V. V. Lebedev (by over 100 times). Moreover, P. I. Klimuk presented an increase in sporulated anaerobic bacteria. After landing, O. I. Klimuk presented disappearance of bifidobacteria. By this time, there was restoration of quantitative content of streptococcus in both cosmonauts. However, proteus content remained somewhat elevated in P. I. Klimuk.

Table 3. Changes in quantity of different representatives of intestinal flora in the crew of Soyuz-13 spacecraft

Group of microorganisms	P.I. Klimuk			V. V. Lebedev		
	day of examination					
	preflight		postflight	preflight		postflight
	20th	1st-3d	1st	20th	1st-3d	1st
Streptococcus	$2,8 \cdot 10^7$	$8,0 \cdot 10^9$	$5,0 \cdot 10^6$	$6,0 \cdot 10^6$	$3,8 \cdot 10^8$	$2,8 \cdot 10^6$
Proteus	$1,0 \cdot 10^2$	$1,0 \cdot 10^3$	$1,0 \cdot 10^4$	$1,0 \cdot 10^3$	$1,0 \cdot 10^3$	$1,0 \cdot 10^3$
Bifidobacteria	$1,5 \cdot 10^9$	$1,0 \cdot 10^8$	None found	$6,0 \cdot 10^8$	$1,1 \cdot 10^7$	$2,0 \cdot 10^8$
Sporulated anaerobic bacilli	$5,7 \cdot 10^6$	$2,1 \cdot 10^7$	$1,0 \cdot 10^5$	$1,6 \cdot 10^5$	None found	None found

The next stage of this study consisted of examining the microbial cenosis of the intestine of cosmonauts involved in long-term space flights. The results revealed that the nature of changes in composition of intestinal flora is analogous to the changes in intestinal microflora after brief flights. Thus, we found a marked decline of lactobacillus content (from $2.2 \cdot 10^7$ to $6.0 \cdot 10^5$) in G. M. Grechko. It should be noted, however, that the changes in lactobacillus content were stable; they did not revert to the base level, even 1 month after conclusion of the flight. In commander A. A. Gubarev, the composition of intestinal microflora was notable for persistent eubiosis in both the preflight and postflight periods.

Examination of intestinal microflora of the crew involved in the second expedition aboard the Salyut-4 orbital station (Table 4) revealed the following: bifidobacteria disappeared and lactobacillus content decreased in the preflight period in P. I. Klimuk. At this time, proteus content was somewhat high, as compared to prior studies. In V. I. Sevast'yanov, there were virtually no changes in intestinal microflora in the preflight period, and the composition thereof was identical to that demonstrated 20 days before the flight, and it was characterized by an increase in sporulated anaerobic bacteria, E. coli and proteus. In P. I. Klimuk, we demonstrated an insignificant (10-fold) increase in sporulated anaerobic bacilli on the 1st postflight day. There was also some increase in proteus content. However, the amounts of these microorganisms reverted to the base level on the 3d postflight day. In spite of the distinct changes in quantity of bifidobacteria and lactobacilli in the preflight period, the amount thereof did not undergo substantial change after the flight, as compared to background data. On the 1st postflight day, we observed normalization of aerobic intestinal flora--a decrease in Escherichia and Proteus--in V. I. Sevast'yanov. Concurrently, there was restoration of the proportion of bifidobacteria and E. coli. As in P. I. Klimuk, there was a high content of sporulated anaerobic bacilli, the number of which reverted to levels inherent in the norm by the 3d postflight day.

Table 4. Changes in quantity of different representatives of intestinal flora in the crew of the second expedition aboard the Salyut-4 orbital station

Group of microorganisms	P.I. Klimuk			V.I. Sevast'yanov		
	day of examination					
	preflight		postflight	preflight		postflight
	20th	1st-3d	1st	20th	1st-3d	1st
Proteus	$1,0 \cdot 10^3$	$1,0 \cdot 10^4$	$1,0 \cdot 10^4$	$1,0 \cdot 10^4$	$1,0 \cdot 10^4$	$1,0 \cdot 10^3$
Lactobacilli	$8,0 \cdot 10^5$	$4,0 \cdot 10^3$	$3,8 \cdot 10^7$	$1,4 \cdot 10^7$	$1,6 \cdot 10^6$	$1,8 \cdot 10^7$
Bifidobacteria	$6,0 \cdot 10^8$	None found	$5,6 \cdot 10^8$	$1,0 \cdot 10^9$	$6,0 \cdot 10^8$	$4,0 \cdot 10^8$
Sporulated anaerobic bacilli	$1,6 \cdot 10^5$	$4,0 \cdot 10^5$	$4,0 \cdot 10^6$	$6,0 \cdot 10^6$	$3,0 \cdot 10^6$	$1,0 \cdot 10^7$

The absence of marked changes in bifidobacteria and lactobacillus content in the postflight period and relatively rapid normalization of intestinal microflora in the cosmonauts were apparently attributable to the beneficial effect of the set of preventive agents used during the flight on intestinal microbial cenosis. In particular, the cosmonauts took food supplements. We observed the beneficial effect of food supplements on composition of intestinal microflora, manifested by an increase in bifidobacterium and lactobacillus content, in ground-based studies involving simulation of nervous and emotional stress.

Thus, the obtained data are indicative, first of all, of the presence of marked changes in microbial cenosis of the intestine in the prelaunch period. The latter is evidently due to the effect of nervous and emotional stress. The disturbances in intestinal biocenosis are manifested by a decrease in bifidobacteria and lactobacilli down to total disappearance in some of the subjects. The obtained data confirmed the results of earlier studies pursued on the ground [1]. It is assumed that stress influences factors that regulate the localization and level of microbial associations in the gastrointestinal tract [1, 9, 10]. Evidently, the lability of intestinal microflora demonstrated in the prelaunch period predetermines the possibility of changes in microbial cenosis during space flights. Thus, even in the case of the brief missions aboard Soyuz-13 and Soyuz-16 spacecraft, a change in bifidobacterium and lactobacillus content was observed. With extension of flight time (first expedition on the Salyut-4 orbital station), these changes could be more stable, as demonstrated in G. M. Grechko. On the other hand, in the presence of stable eubiosis in A. A. Gubarev in the preflight period (including prelaunch), there were no dysbiotic changes in intestinal microbiocenosis after he landed.

We must mention the beneficial effect on intestinal microbial cenosis of the set of preventive measures used during the 63-day space flight.

Thus, on the basis of the obtained results, we can conclude that bifidobacteria and lactobacilli are the most susceptible to change under extreme conditions. For this reason, it is imperative to institute treatment of intestinal microflora for preventive purposes, to maintain stability of bifidobacteria and lactobacilli. It is desirable to use products derived from the above-mentioned microorganisms, as well as to include in the diet both sour milk products based on special ferments, as well as alimentary factors favoring reproduction of bifidobacteria.

BIBLIOGRAPHY

1. Liz'ko, N. N. "Change in Composition of Normal Intestinal Microflora Related to Different Diets and During a Long Stay in a Sealed Area," candidatorial dissertation, Moscow, 1969.

2. Shilov, V. M.; Liz'ko, N. N.; Bragina, M. P.; et al. in "Kosmicheskaya biologiya i aviakosmicheskaya meditsina" [Space Biology and Aerospace Medicine], Moscow--Kaluga, Vol 1, 1972, p 235.

3. Shilov, V. M., and Liz'ko, N. N. ERNAHRUNGSFORSCHUNG, Vol 18, 1974, p 305.

4. Zaloguyev, S. N.; Shinkareva, M. M.; and Utkina, T. G. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1970, p 54.

5. Bengson, M. B. AM. J. CLIN. NUTR., Vol 23, 1970, p 1525.

6. Brockett, R. M., et al. in "Skylab Life Sciences Symposium," proceedings, Houston, Vol 1, 1974, p 121.

7. Taylor, C. R., and Zaloguev, S. N. in "Medical Microbiology Analyses of Apollo-Soyuz Test Project NASA," Houston, 1976, p 22.

8. Liz'ko, N. N.; Shilov, V. M.; and Merkova, T. I. in "Epidemiologiya, klinika, profilaktika i lecheniye ostrykh i khronicheskikh kishechnykh infektsiy" [Epidemiology, Symptomatology, Prevention and Treatment of Acute and Chronic Intestinal Infections], Moscow, 1975, p 98.

9. Holdeman, L. V.; Good, I. J.; and Moore, W. E. C. APPL ENVIRONM. MICROBIOL., Vol 31, 1976, p 359.

10. Tannock, G. W., and Savage, D. C. INFECT. AND IMMUN., Vol 9, 1974, p 591.

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SOME OF THE PRINCIPLES INVOLVED IN SANITARY AND HOUSEKEEPING ARRANGEMENTS IN SPACECRAFT

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[Article by S. N. Zaloguyev, V. V. Borshchenko, A. N. Viktorov, A. G. Prishchep and G. A. Shumilina, submitted 25 Jul 77]

[English abstract from source]

Significant changes in the functional state of crewmembers during prolonged space missions necessitate corrections to be made in the scope and methods of sanitation and housekeeping arrangements. Due to the fact that in space flight automicroflora representatives may acquire greater importance as possible pathogenic agents, procedures providing body cleanliness should include both physico-chemical exposures and direct skin microflora treatment. On the basis of pertinent investigations the authors have developed selection criteria and requirements for detergents and disinfectants that may be used in prolonged space flights.

[Text] The approach to elaboration of the principles involved in sanitary and housekeeping provisions for cosmonauts is presently based on extensive factual material obtained during preparation and implementation of manned space flights [1-6]. However, with increase in time spent by humans in spacecraft, the scope and methods of sanitation and housekeeping require substantial change, in view of the fact that there is information concerning the possibility of appearance of significant changes in the functional state of cosmonauts [7, 8].

Our objective here is to substantiate some of the principles involved in sanitation and housekeeping arrangements in spacecraft that function for long periods of time.

Methods

In this study, we used the results of numerous investigations pursued in sealed chambers with the participation of humans, as well as during the actual space flights aboard Soyuz spacecraft and Salyut orbital stations.

We examined the quantitative and qualitative composition of microflora of the human integument using methods that were described previously [9, 10]. In addition, we measured lipid content of the skin (method of Yu. F. Korolev), intensity of accumulation of chlorides, concentration of hydrogen ions and other parameters [11].

Results and Discussion

When people are confined to pressurized cabins of spacecraft, they are exposed to a speific set of space factors [12] that induce functional changes in a number of systems and organs [13].

Of special interest to development of principles of sanitary and housekeeping equipment for space missions are the changes in quantitative and qualitative composition of automicroflora of the integument, which are associated with changes in nonspecific resistance of man to diseases [14]. There is a significant increase here in the role played by such representatives of the automicroflora as staphylococci, streptococci, Gram-negative bacilli of the general Klebsiella and Pseudomonas, yeast-like fungi of the genus Candida as possible pathogens [15, 16].

A very marked increase in extensiveness of microbial sites is observed on the integument of individuals confined to pressurized cabins, and as a result there is significant increase in intensity of discharge of microorganisms into the environment. It was demonstrated that, while man discharges an average of 110 microorganisms per hour from the upper respiratory tract under ordinary conditions, the figure is 10 times higher when confined to an airtight space. There are analagous changes with regard to the human integument. The discharge of microorganisms is 10-150 times higher in an airtight space than under ordinary circumstances. The limited personal hygiene measures are one of the main factors determining the nature and intensity of changes in discharge of microorganisms. This is one of the causes of accumulation of microorganisms in the environment of pressurized cabins and increase in role of air, internal surfaces, as well as life support systems as the main factors in transmission of pathogenic representatives of human automicroflora [17].

Thus, development of an optimum system of measures referable to sanitation and housekeeping is closely related to problems of sanitary bacteriology, since the possibility of onset of a disease of the "autoinfection" type or expression of a mechanism at the basis of "cross infection" is determined by the distinctive features of personal hygiene measures used, as well as effectiveness of clearing microorganisms from the atmosphere of a cabin.

Sanitary and housekeeping "support" can be defined as a set of procedures of personal hygiene performed by cosmonauts, as well as maintenance of optimum sanitary-hygienic and anti-epidemic conditions in the cabin.

The main direction of measures for personal hygiene is to maintain body cleanliness, preserve products of vital functions that are stored and then to process or dispose of them.

In view of the fact that the role of automicroflora increases significantly as possible pathogens of diseases when man is confined to spacecraft, the procedures for keeping a clean body and caring for it should include those directed toward maintaining an optimum state of integumental microflora, along with physicochemical treatment (hygienic shower, washing the hands, face, etc.). The following goals should be pursued: normalization of quantitative indices of microorganisms on the integument and oral mucosa, lowering the intensity of discharge of microorganisms from the integument into the environment, lowering the risk of expression of the mechanism of transmission of microorganisms, as well as development of autoinfection. In this case, it is desirable to develop both nonspecific (mechanical removal of microorganisms, use of appropriate fabrics for clothing, linens, etc.) and specific methods (use of various bactericidal agents chosen with due consideration of the distinctions of change in automicroflora of cosmonauts), as well as methods directed toward activating the barrier function of the skin and mucous membranes.

Of course, total safety to man, as well as compatibility with living conditions in a spacecraft cabin and life support systems, are the main prerequisites for the personal hygiene measures developed for cosmonauts [18, 19]. This limits significantly the choice of existing measures and requires development of new agents. For this reason, in the space flights performed in the USSR and United States, the scope and nature of measures for personal hygiene of crew members presented certain distinctions, determined mainly by the limitations referable to energy and water supply, weight and dimensions.

Personal hygiene aborad the Soyuz series of spacecraft and Salyut orbital stations included daily sponging of the hands and face, and the mouth, with moist washcloths. Underwear was changed once a week, and this was preceded by rubbing the skin with wet and dry towels. Wet washcloths were also used to clean the hands before meals, after use of toilet facilities ["waste management system"] and to clean the skin at the site of application of electrodes from medical equipment. A special formula lotion with antimicrobial properties was used to dampen the washcloths [5].

It was proven that the personal hygiene supplies, consisting of a set of washcloths and towels moistened with special lotion, are essentially effective enough to remove products of vital functions and exogenous impurities from the human integument. For example, an average of 99 mg chlorides, 105 mg ammonia and 0.7 mg nitrites were removed from the face and hands with the use of a single washcloth. The used washcloth contained 1060 mg organic matter (scaled to osygen) and a large amount of microorganisms. The cleansing and refreshing effect of using washcloths and towels on the skin corresponded to the requirements of maintaining the initial functional level of this organ. The lack of morphological manifestations of skin diseases among crew members of Soyuz spacecraft and Salyut orbital stations can serve as a confirmation of this assumption. It should be noted that knitted-fabric underwear absorbed a significant part of the impurities and microorganisms from the skin while it was worn.

However, the set of personal hygiene measures used until recently cannot be considered adequate for longer periods of confinement of man in airtight areas. The data obtained from studies under flight-simulating conditions established that there is very intensive accumulation of chlorides on the subjects' skin toward the end of a 30-day period, with almost 30% decrease in lipid levels and other distinctions. This circumstance, as well as the necessity of periodic treatment not only of smooth surfaces, but those covered with hair, as well as the mouth, require development of new and more effective means of personal hygiene in the course of long-term flights.

The possibility of making regular use during space flights of a system utilizing water (showers, washing, etc.) raises the problem of developing agents with high enough detergent properties and a good disinfectant effect. The specifications for detergent and disinfectant products should include optimum foaming to remove products of vital functions and exogenous impurities without adverse effectz on the function of the skin and its appendages. In this case, the concentration of hydrogen ions, rate of shedding of the epidermis, absence of allergic, sensitizing and other adverse reactions are indices of normal skin function.

The problem of choice of washing and disinfectant products with due consideration of their antimicrobial activity is quite complex. The optimum product would be one that has antimicrobial activity against various representatives of the human autoflora and that precludes development of dysbacteriosis.

However, it is undesirable to use products in the course of long term flights that have a predominant effect on some groups of representatives of the microflora (for example, hexachlorophene, which is effecitve mainly against coccal forms), since they could lead to reproduction of Gram-negative bacteria. One must also take into consideration the possibility of habituation of bacteria to antimicrobial products. This probability has been proven for hexachlorophene, with regard to staphylococcus, E. coli, etc. [20]. For this reason, it is desirable to use a combination of several products, and this is particularly important to provide for oral hygiene and hygiene of the body areas covered with hair.

One of the specifications that could be set for detergents and disinfectants recommended for cosmonaut personal hygiene is the capacity to exert a prolonged antimicrobial action in low concentrations, in order to prevent reproduction of microorganisms in the case where these products are stored for a long time before being added to the water regeneration system. The latter circumstance (which could limit, to some extent, the choice of detergent-disinfectant formulas, must be taken into consideration) makes it necessary for these products to be compatible with the systems for regeneration of water used for sanitary and housekeeping purposes and removal of components that are not included in the pure water standards.

The solution of these problems should aid in creating optimum sanitary and hygienic conditions for cosmonaut work and nonwork activities ["housekeeping"].

BIBLIOGRAPHY

1. Levashov, V. V. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 4, 1965, pp 165-168.

2. Levashov, V. V., and Finogenov, A. M. in "Problemy kosmicheskoy biologii i meditsiny" [Problems of Space Biology and Medicine], Moscow, Vol 7, 1967, pp 420-424.

3. Finogenova, A. M., et al. in "Osnova kosmicheskoy biologii i meditsiny" [Foundation of Space Biology and Medicine], Moscow, Vol 3, 1975, pp 122-140.

4. Borshchenko, V. V. Ibid, pp 141-164.

5. Nefedov, Yu. G., et al. in "Kosmicheskiye polety na korablyakh 'Soyuz.' Biomeditsinskiye issledovaniya" [Space Missions Aboard Soyuz Spacecraft. Biomedical Studies], Moscow, 1976, pp 41-64.

6. Giotta, A. J. AIAA Paper, No 878, 1971.

7. Gazenko, O. G. VESTN. AN SSSR [Vestnik of the USSR Academy of Sciences], No 4, 1976, pp 25-36.

8. Berry, Ch. A. AEROSPACE MED., Vol 41, 1970, pp 500-519.

9. Zaloguyev, S. N., et al. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1970, pp 54-59.

10. Viktorov, A. N. "Means of Dissemination of Microorganisms in an Airtight Habitat Occupied by Man for a Long Time," candidatorial dissertation, Moscow, 1971.

11. Popov, I. G.; Borshchenko, V. V.; et al. in "Problemy kosmicheskoy biologii i meditsiny," Moscow, Vol 7, 1967, pp 413-420.

12. Lebedinskiy, A. V., et al. in "Konferentsiya po kosmicheskoy biologii i meditsiny. Materialy" [Conference on Space Biology and Medicine. Proceedings], Moscow, 1966, pp 3-10.

13. Pestov, I. D., and Geratevol', Z. Dzh. in "Osnovy kosmicheskoy biologii i meditsiny," Moscow, Vol 2, Bk 1, 1975, pp 324-369.

14. Nefedov, Yu. G., et al. in "Life Sciences and Space Research," Berlin, Vol 9, 1971, pp 11-16.

15. Startseva, N. D. in "Aktual'nyye voprosy kosmicheskoy biologii i meditsiny" [Pressing Problems of Space Biology and Medicine], Moscow, 1975, pp 214-215.

16. Taylor, G. R., and Henny, M. R. APPL. MICROBIOL., Vol 26, 1973, pp 804-813.

17. Nefedov, Yu. G., et al. KOSMICHESKAYA BIOL., No 4, 1975, pp 19-23.

18. Rosener, A. A., et al. AIAA Paper, No 873, 1971.

19. Gaydadymov, V. B., et al. KOSMICHESKAYA BIOL., No 1, 1976, pp 73-75.

20. Evans, Z. A., et al. J. INVEST. DERM., Vol 60, 1973, pp 207-214.

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OBJECTIVES AND CONDITIONS OF PHYSIOLOGICAL EXPERIMENTS ON RATS CONDUCTED ABOARD THE COSMOS-936 BIOSATELLITE

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[Article by Ye. A. Il'in, V. I. Korol'kov, A. R. Kotovskaya, A. D. Noskin, V. A. Kondrat'yeva, A. A. Shipov and I. I. Britvan, submitted 4 Apr 79]

[English abstract from source]

The paper describes the basic goals and experimental conditions of physiological studies of rats flown aboard the Soviet biological satellite Cosmos-936.

[Text] With development of manned fights, biological experiments in space do not lose their scientific and applied importance. Such experiments make it possible to conduct more comprehensive and deeper studies of reactions of living organisms to space environment conditions. As time passed, biological experiments in space also began to acquire independent significance, being the source of basic scientific information.

Numerous experiments on microorganisms, plants, insects, fish and mammals, which were conducted in manned spacecraft and biosatellites, failed to demonstrate the deleterious effect of long-term weightlessness on intracellular biological processes, including those related to transmission of genetic information and cell division [1-5]. At the same time, several rather serious structural and functional changes were noted, for which reason comparative studies were begun, through experiments on the Cosmos-782 biosatellite, of the effects of weightlessness and artificial gravity (AG) on basic processes of vital functions.

Analysis of the results obtained revealed that the biological effects of AG constituting 1 G, generated during the space flight by rotation of the onboard centrifuge, are identical in direction to the effect of natural (earth's) gravity. This data warranted consideration of AG as one of the effective means of preventing the adverse effect of weightlessness. It was deemed important to continue the studies using experimental objects with higher organization, i.e., laboratory rats.

The main objectives of experiments with mammals (rats) during the 18.5-day flight aboard the Cosmos-936 biosatellite (3-22 Aug 77) were to further investigate the mechanisms of physiological effects of weightlessness, substantiation of AG as a means of preventing the adverse effects of weightlessness, as well as to assess the possibility of forming a group of control animals in experiments aboard biosatellites that would be exposed to all space flight factors, with the exception of weightlessness. The existence of such a group of animals would make it possible to differentiate better between the influence of weightlessness on physiological systems and the effects of other factors associated with space flights.

The experiments aboard Cosmos-936 were conducted on male Wistar-SPF rats supplied by the Institute of Endocrinology, Slovak Academy of Sciences (Bratislava, CSSR).

For the flight experiment and vivarium control, we used animals delivered to the Institute of Biomedical Problems, USSR Ministry of Health, at the age of 35-36 days, weighing 110 g, and for the synchronous control experiment we used animals that were 32-33 days old and weighed 90-100 g.

Rats were screened on the basis of findings of daily clinical examination, dynamics of weight gain, morphological composition of peripheral blood, microbiological examination of the throat [or mouth] and bactericidal activity of the skin on the tail, otoscopy, as well as results of studying behavioral reactions.

We selected clinically healthy rats of about the same weight out of the entire batch. At the start of the experiment, the rats weighed an average of 214.8 g and they were 9 weeks old.

The flight experiment was preceded by a clinicophysiological examination, surgical interventions (implantation of body temperature and bone matrix biosensors, delabyrinthation of a group of rats), injections (^{14}C-glycine, declomycin, 10% sheep erythrocyte suspension), screening and training of animals. This period lasted 30 days.

The Table lists the typical distinctions of animal groups used in the flight experiment.

In the preflight period, the animals were kept under vivarium conditions in stationary polyvinyl cages, 450×310×160 mm in size, with 5 rats in each.

All of the cages were cleaned once a day, in the morning, before feeding the animals. Air temperature in the vivarium constituted 22±2°C, relative humidity was 80±5%, with 12 h of daylight.

The animals were switched from pellets to homogenized pasty feed, which was given once a day, at the rate of 40 g per rat, 15 days prior to the start of the flight and synchronous experiments.

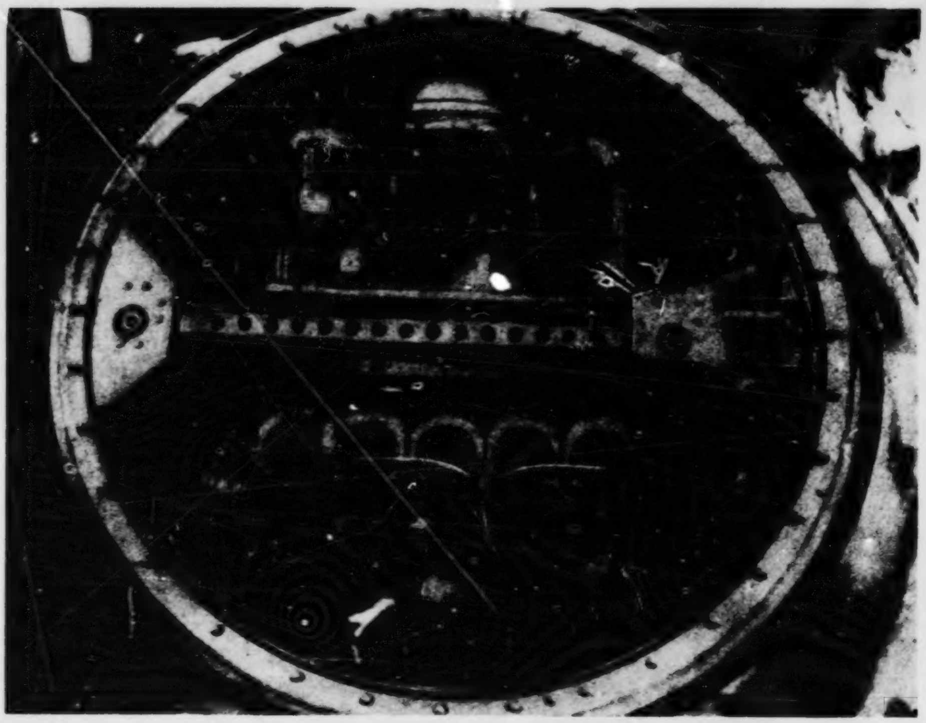
Distribution of anima-s in groups in the flight (F) experiment aboard Cosmos-936 biosatellite

	Animal groups					
	on centrifuges [C]		in weightlessness [W]			
	FC$_1$	FC$_2$	FW$_1$	FW$_2$	FW$_3$	FW$_4$
Number of snimals	5	5	5	5	5	5
Initial weight	209,3±3,1	216,8±1,6	207,3±2,4	206,8±2,1	214,8±1,6	202,8±5,2
Surgical intervention	—	Implantation of body temp. sensors in abdominal cavity	—	Implantation of decalcified and lyophilized bone matrix under fascia of anterial wall of abdomen	Implantation of body temp. sensors in abdominal cavity	Bilateral delabyrinthation
Injections	Declomycin (twice)	Declomycin (twice). ^{14}C-glycine	Declomycin (twice)	Declomycin (twice), 10% sheep erythrocytes	Declomycine (twice), ^{14}C-glycine	
Time animals were sacrificed	R + 0	R + 25	R + 0	R + 0	R + 25	R + 25

The animals selected for the experiments were conditioned to staying in functional mockups of automated maintenance systems. Conditioning lasted a total of 30 h.

Final screening of animals for the experiments was made after completing all types of surgical interventions, background clinical and physiological studies and completion of training [conditioning].

In all, there were 30 rats aboard Cosmos-936, 20 of which under weightless conditions (groups FW_1, FW_2, FW_3 and FW_4) and 10 were on two centrifuges (groups FC_1 and FC_2; see Figure). The rats that were weightless during the flight were kept in automated systems which were similar in design to the systems previously used aboard Cosmos-605, Cosmos-690 and Cosmos-782 biosatellites [1, 2, 4].



General arrangement of onboard centrigues and stationary animal containers in biosatellite mockup (one centrifuge and one unit for five animals can be seen)

The animal upkeep conditions on the centrifuges were virtually the same as for rats in weightlessness. The rate of centrifuge rotation during flight constituted 53.5±3 r/min, and AG constituted 1 G on a radius of 320 mm (to the arbitrary longitudinal axis of the animal).

The centrifuges began to rotate immediately after the biosatellite was inserted in a near-earth orbit and they were stopped 4 h 45 min prior to landing on earth.

During the flight, the following microclimate parameters were maintained in the biosatellite's pressurized cabin: 145-210 mm Hg pO_2, no more than 14 mm Hg pCO_2, 21.5-24.0°C temperature and 80-90% relative humidity.

A field laboratory was deployed at the landing site to perform biological, physiological, morphological and biochemical tests.

Concurrently with the flight, with a 4-day shift, a synchronous ground-based experiment was conducted in a mockup of the landing biosatellite; in this mockup, we reproduced the habitat of the animals aboard the Cosmos-936 biosatellite and the dynamic factors inherent in the insertion, descent from orbit and landing phases. The distribution of animals in groups in the synchronous experiment was the same as in the flight experiment (groups SC_1, SC_2, SW_1, SW_2, SW_3, SW_4).

To analyze the effects of rotation factors on the physiological parameters studied, concurrently with the synchronous experiment we conducted an experiment on two centrifuges, the radius of rotation of which constituted 92 mm (groups C_1^0 and C_2^0, with 5 animals in each). The rate of rotation of the short-radius centrifuges was the same as for the onboard centrigues.

The levels of toxic gas impurities in the air environment of the biosatellite pressurized cabin did not exceed the permissible concentrations.

The microflora of the air environment was represented by nonpathogenic forms of microorganisms, mainly staphylococci and micrococci. No microorganisms of the enteric group were demonstrable. Consequently, the animal upkeep systems used provided for rather effective protection of the internal environment of the biosatellite and its mockup against access of microorganisms, the sources of which could have been the animals.

The first stage of the studies was begun 3.5 h after the biosatellite descent vehicle landed.

On the day the flight ended, 10 rats that had been under weightless conditions (groups FW_1 and FW_2) and 5 rats that had been on the centrifuge (group FC_1) were sacrificed for morphological and biochemical studies. The remaining animals were submitted to physiological examination at different stages of readaptation. These animals were sacrificed for morphological and biochemical studies on the 25th postflight day (see Table).

The physiological studies conducted in the postflight period included a physical examination of the animals, weighing, testing equilibrium and static endurance, overturning and landing reflex, latency period of lift reaction, characteristics of vestibular nystagmus and higher nervous activity. We also examined the morphological composition of peripheral blood, gas-energy metabolism, body temperature, life span of erythrocytes and conducted microbiological tests.

Specialists from Bulgaria, Hungary, the German Democratic Republic, Poland, Romania, Czechoslovakia, the United States and France participated in examining the biological material from rats and analyzing the obtained results.

BIBLIOGRAPHY

1. Il'in, Ye. A.; Serova, L. V.; and Noskin, A. D. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1976, pp 9-14.

2. Grigor'yev, Yu. G.; Druzhinin, Yu. P.; Verigo, V. V.; et al. Ibid, No 5, 1977, pp 58-66.

3. Platonova, R. N.; Parfenov, G. P.; Ol'khovenko, V. P.; et al. IZV. AN SSSR. SER. BIOL. [News of the USSR Academy of Sciences, Biology Series], No 5, 1977, pp 770-775.

4. Gazenko, O. G.; Genin, A. M.; Il'in, Ye. A.; et al. KOSMICHESKAYA BIOL., No 6, 1978, pp 43-49.

5. Portugalov, V. V. IZV. AN SSSR. SER. BIOL., No 4, 1978, pp 501-506.

UDC: 612.8.015.2-06:629.78

SOME NEUROCHEMICAL CHARACTERISTICS OF RATS DURING FLIGHT ABOARD THE COSMOS-782 ARTIFICIAL SATELLITE AND AFTER RETURN TO EARTH

Moscow KOSMICHESKAYA PIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 6, 1979 pp 22-26

[Article by O. G. Gazenko, N. N. Demin, A. N. Panov, D. A. Rashevskaya, N. L. Rubinskaya and R. A. Tigranyan, submitted 23 Feb 77]

[English abstract from source]

The brain of rats flown aboard the biosatellite Cosmos-782 was sampled immediately postflight and taken under neurochemical study. It was shown cytospectrophotometrically that the absolute content of RNA decreased by 20% in the cytoplasm of cerebellar Purkinje cells and remained unaltered in glial cells-satellites, and that the protein content did not change. In the frontal cortex (homogenates) the concentration of sulfhydryl groups decreased by 26%, activity of nonspecific cholinesterase by 30% and acetyl cholinesterase by 33%. The activity of the latter in the cerebellum also diminished.

[Text] The distinctive feature of the biological experiment conducted aboard Cosmos-782 artificial satellite was that it was possible to start examining the animals (rats) or fix material right at the landing site. We could assume that the metabolic changes inherent in flight conditions did not yet have time to change under the influence of returning to earth's gravity, or to become distorted due to stress during long-term transportation.

We selected the following parameters as neurochemical indices of the state of the brain: RNA and protein content of Purkinje cell cytoplasm and their glial cerebellar satellite cells; sulfhydryl group content of cerebellar tissue, mesencephalong and cerebral cortex, as well as cholinesterase activity of these regions.

Changes in total protein and RNA content of different cells reflect their functional activity [1-3]. One can also assess cell function according to SH group content, since it is closely related to conformational changes in proteins, including structural ones, while the conformation of protein molecules is largely determined by the proportion of reduced and oxidized SH groups [4-7]. Finally, activity of the enzyme that specifically splits acetylcholine (acetylochoinesterase--ACE, EC 3.1.1.7) can be indicative of neuronal capacity to transmit excitation; the activity of nonspecific acylhydrolase of acylcholines (nonspecific cholinesterase--CE, EC 3.1.1.8) is related primarily to activity of glial cells.

Methods

In order to assay total proteins and RNA in individual cells, samples were fixed in cooled Brodskiy fixing agent then imbedded in paraffin [1]. After deparaffination, proteins in sections 608 μm in thickness were stained with amido black 10-B [8] and RNA with gallocyanin-chromium alum [9]. The concentration of the assayed substances was determined by means of cytospectrophotometry, according to magnitude of optical density in neuronal cytoplasm and gliocytes for a beam at a specific wavelength. For this purpose, we used a two-beam MUF-5 probing cytospectrophotometer, at a wavelength of 620 nm for proteins and 585 nm for RNA. Optical density was measured in 2-4 cell areas. To determine the absolute amount of tested component per cell, we measured the cell volumes by which we then multiplied the obtained optical density values [10, 11].

SH group content of homogenates of the different parts of the brain was determined amperometrically, with titration with silver nitrate solution [12]. This results in reaction of both protein SH groups and SH groups of low molecular nonprotein compounds. However, the levels of the latter are negligible, and most of the demonstrable SH groups in tissue homogenates are referable to structural proteins.

We used the Ellman method [13] to determine ACE and CE activity.

Results and Discussion

Figure 1 illustrates the average results of assaying RNA and total proteins in cerebellar Purkinje cells and their glial satellite cells in animals sacrificed immediately after landing and after 26 days of subsequent upkeep on the ground. In the Table, these data are set against the levels inherent in animals in the synchronous experiment.

Immediately after landing, changes (in the direction of decline) in both concentration and absolute amount of RNA were demonstrated only in the neuronal bodies, but not the gliocytes. There was a 17% drop in concentration of RNA in rat Purkinje cells after the flight, as compared to the vivarium control, and a 14% drop as compared to animals in the synchronous experiment. There was a decline in absolute RNA content of neurons in both flight rats (by 20%) and animals in the synchronous control (by 10%); in the latter case, no reliable differences between parameters of flight rats and those in the synchronous control were demonstrated.

There was no change in either amount or concentration of proteins in both the neurons and cerebellar glial cells in the examined groups of animals.

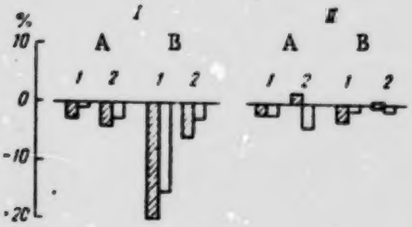


Figure 1. Absolute protein and RNA content (per cell) in cytoplasm of Purkinje cells of the cerebellum and their glial satellite cells. Striped columns--rats aboard Cosmos-782, white columns--animals aboard Cosmos-605

A) proteins B) RNA 1) Purkinje cells 2) gliocytes

Here and in Figures 2 and 3: I) immediately after landing
II) 26 days after flight

Absolute RNA and protein content of Purkinje cells and their glial satellite cells in cerebellum of rats aboard Cosmos-782 artificial satellite, % vivarium control

Component and type of cell	Satellite		Synchronous control	
	optic density	absolute content	optic density	absolute content
Immediately after landing				
RNA:				
Purkinje cells	—17	—20	—4	—10
glia	—6	—6	+3	+3
Proteins:				
Purkinje cells	0	—3	+3	—4
glia	—4	—4	+1	+1
26 days after flight				
RNA:				
Purkinje cells	—4	—3	—4	—3
glia	0	0	—6	—5
Proteins:				
Purkinje cells	—3	—2	—2	—1
glia	+2	+2	+2	+3

There were no changes whatsoever in the parameters studied, as compared to the vivarium control, 26 days after landing.

Upon comparing the data obtained from testing tissue samples taken directly at the landing site to those obtained on animals flown aboard Cosmos-605, transported and then sacrificed 1 day after landing, we were impressed by the virtually identical protein and RNA content of cerebellar cells (see Figure 1). Consequently, the changes demonstrated in both the last and preceding experiments are the result of rather profound and persistant changes in neuronal metabolism, induced expressly by exposure to flight conditions (and, to some extent, by accelerations during the landing phase). These changes did not change, even after 1 day, during which the rats were exposed to additional stress factors.

Figure 2 illustrates data pertaining to SH group content of homogenates of the frontal cerebral cortex (% of control). The base values were obtained from testing rats maintained under usual vivarium conditions (vivarium control). In the control, the levels expressed in micromoles per 100 mg wet weight constituted 0.66±0.01, 0.65±0.01, 0.52±0.01 and 0.63±0.01 in the frontal and occipital cortex, mesencephalon and cerebellum, respectively. There was no reliable difference in protein content of the regions examined.

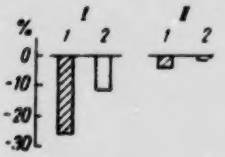


Figure 2.
SH group content in frontal cortex homogenates

1) flight animals
2) animals in synchronous control

Right after landing, there was a significant decrease (by 26% as compared to the vivarium control and 14% as compared to synchronous control) in SH groups, but only in the frontal region. As compared to the vivarium control, there was a 12% drop in SH group content of the same region in the synchronous control.

In the brain regions studied, there was no difference in SH group content 26 days after landing, as compared to the levels inherent in the vivarium control.

Figure 3 illustrates data on ACE and CE activity in experimental animals. In the vivarium control, the enzyme activity of which was taken as 100%, the absolute values for ACE constituted 1397±35, 895±22, 2924±44 and 788±19 μM acetylthiocholine split in 1 h, scaled to 1 g wet tissue, in the frontal and occipital regions, mesencephalon and cerebellum, respectively. CE activity in this regions constituted 43±2.3, 42±1.8, 12.4±4.0 and 41±2.9.

Immediately after landing, ACE activity in flight animals was reliably diminished in the frontal cortex and cerebellum (by 33 and 10%, respectively), and CE activity was diminished in the frontal and occipital cortex (by 30 and 31%, respectively) and in the cerebellum (by 27%). In the synchronous control, a reliable decrease in ACE activity was observed only in the frontal cortex (by 12%), while CE activity in the mesencephalon even increased somewhat (by 10%), remaining unchanged in other parts of the brain.

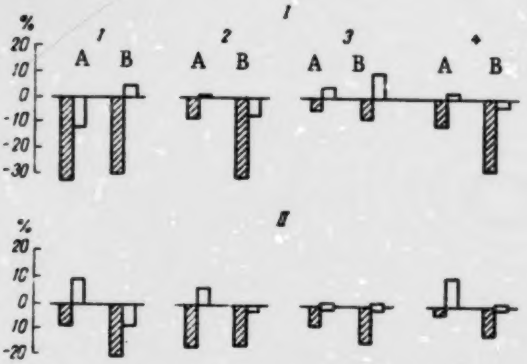


Figure 3.
Acetylcholinesterase and nonspecific cholinesterase activity. Striped columns--"flight" animals; white columns--animals in synchronous control

A) ACE activity B) CE activity

1) frontal cortex
2) occipital region
3) mesencephalon
4) cerebellum

A reliable decrease in ACE and CE activity in flight animals was demonstrated 26 days after landing in the occipital cortex (by 17 and 16%, respectively) and mesencephalon (8 and 14%, respectively). The observed decrease in ACE and, particularly, CE in the frontal cortex was found to be unreliable.

On the basis of these findings, it can be concluded that the changes in cholinesterase activity demonstrated immediately after landing diminished significantly in the 26 days the animals spent on the ground.

From the submitted data it can be concluded that the conditions involved in a long-term space flight (weightlessness, isolation, limited mobility and others) induced some depression of cerebral metabolism in the rats, and this was particularly marked in the regions whose function is related to motor activity--the cerebellum and motor (frontal) cortex. The drop in absolute RNA content of cerebellar Purkinje cells, with retention of the usual protein content, is indicative of diminished protein metabolism in these neurons, i.e., "extinction" of their function. This is also indicated by the decrease in ACE and CE activity. There was a decrease in both SH group content and ACE and CE activity in the motor cortex; both could reflect functional inactivation of central structures. A similar decrease in ACE activity had been demonstrated in the brain of rats whose movements were restricted for 30 days [14].

We were impressed by the fact that the SH group content and activity of ACE (an enzyme related to neurons) in the frontal cortex of animals in the synchronous control were still reliably lower than in the vivarium control, although higher than in flight rats. Probably limited mobility is involved here. It is important that such a difference between the synchronous control and vivarium control was not demonstrable. Hence, it can be concluded that the changes in cerebral metabolism of flight animals were primarily the result of exposure to space flight conditions, but they occurred in the same direction as in the synchronous control.

Returning the animals to the usual terrestrial conditions led essentially to normalization of the aspects of brain metabolism we studied, which had been somewhat impaired in rats examined immediately after landing.

BIBLIOGRAPHY

1. Brodskiy, V. Ya. "Cellular Trophics," Moscow, 1966.

2. Pevzner, L. Z. "Functional Biochemistry of Neuroglia," Leningrad, 1972.

3. Hyden, H. in "The Cell," New York, Vol 4, Pt 1, 1960, pp 215-323.

4. Koshtoyants, Kh. S. "Protein Bodies, Metabolism and Neural Regulation," Moscow, 1951.

5. Torchinskiy, Yu. M. "Sulfhydryl and Disulfide Groups of Proteins," Moscow, 1971.

6. Glazer, A. N. ANN. REV. BIOCHEM., Vol 39, 1970, pp 101-130.

7. Rothstein, A. in "Current Topics in Membranes and Transport," New York, Vol 1, 1970, pp 135-176.

8. Geyer, G. ACTA HISTOCHEM. (Jena), Vol 10, 1960, pp 286-292.

9. Berube, G. R.; Powers, M. M.; Kerkay, J.; et al. STAIN TECHNOL., Vol 41, 1966, pp 73-81.

10. Voronka, G. Sh.; Demin, N. N.; and Pevzner, L. Z. DOKL. AN SSSR [Reports of the USSR Academy of Sciences], Vol 198, No 4, 1971, pp 974-977.

11. Voronka, G. Sh.; Demin, N. N.; Rubinskaya, N. L.; et al. UKR. BIOKHIM. ZH. [Ukrainian Biochemical Journal], No 6, 1972, pp 712-717.

12. Sokolovskiy, V. V. LABOR. DELO [Laboratory Record], No 8, 1962, pp 3-6.

13. Ellman, G. L. ARCH. BIOCHEM., Vol 82, 1959, pp 70-77.

14. Korneyeva, N. V. "The Acetylocholine-Cholinesterase System of Brain Tissue and Certain Other Rat Organs With Exposure to Diverse Extreme Factors," author abstract of candidatorial dissertation, Moscow, 1970.

UDC: 616-02:612.014.477-064]-085.825.
6-07:616-008.92-074

EFFECTS OF MINIMAL GRAVITATIONAL LOADS ON FLUID-ELECTROLYTE METABOLISM AND RENAL FUNCTION OF MAN DURING PROLONGED IMMERSION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 6, 1979 pp 27-31

[Article by A. I. Grigor'yev and Ye. B. Shul'zhenko, submitted 14 Apr 77]

[English abstract from source]

It was demonstrated that renal excretion of fluid, osmotically active substances and electrolytes could be reduced, using low gravitational exposures ($+G_z$). The degree and duration of water and electrolyte retention were different with respect to the experimental time. The major physiological mechanisms of the changes in fluid-electrolyte metabolism were a decrease in the glomerular filtration rate and a change in water and ion transport in renal tubules.

[Text] Various remedies have been proposed [1-4] to prevent disorders of fluid-electrolyte metabolism and renal function, which occur during and after space flights. However, they do not prevent entirely signs of hypohydration and electrolyte deficiency that are inherent in weightlessness, which makes it necessary to continue research in this direction. On the basis of the suggestion offered by White [5], that it is necessary to use measured rotation on a centrifuge to increase the body's resistance to weightlessness, we tried to evaluate the efficacy of this measure in model studies, for the purpose of possible correction of changes in fluid-electrolyte balance. We have studied here the influence of periodic gravity loads ($+G_z$) of minimal levels on fluid-electrolyte metabolism, osmoregulatory and ion-regulatory renal functions of a healthy man during long-term immersion.

Methods

We studied 10 healthy male volunteers ranging in age from 25 to 39 years; they remained immersed for 13 days. The method, which is based on the principle of "dry" submersion, as well as experimental conditions have been described previously [6]. The subjects were divided into two groups, with five men in each. The first group of subjects was submitted to "head-pelvis" accelerations of 0.6-2.0 G for 60-90 min a day (1000 to 1300 hours) starting on the 8th day of immersion. We used +3 G accelerations for 5 min before and right after immersion as a functional load test. A centrifuge with a radius of 7.25 m, with an acceleration build-up gradient of 0.2 G/s was used for all rotations. The second group of subjects (control) spent the entire period of investigation in "pure" immersion.

Renal function was tested for 3 days in the background period, daily during immersion and for 11 days of the recovery period. The subjects were hospitalized during the background and recovery periods, and they were kept on a standard diet. At all stages of the study, there were no restrictions on fluid intake, but a strict record thereof was kept. Batches of urine were collected daily. Venous blood samples were taken twice in the background period and numerous times during immersion and in the recovery period. In all samples of blood serum and urine determination was made of sodium and potassium content by the method of flame photometry (PFM-1), calcium and magnesium were assayed spectrophotometrically, creatinine was assayed according to (Bonsnes-Toska), urea with paradimethylbenzaldehyde, and osmotic concentration by the cryoscopy method with an MT-54M semiconductor thermistor. The results of the tests were processed by the method of variation statistics for small samples.

Results and Discussion

Fluid intake decreased and fluid output increased ($P<0.02$) in all subjects during the first 2 days after submersion in the immersion medium, and this led to a difference of an average of 600-900 mℓ/day ($P<0.001$) between diuresis and fluid intake. During this period, we also observed increased excretion by the kidneys of osmotically active substances ($P<0.05$), including sodium ions ($P<0.05$, Figure 1). This was associated with a decline of osmotic concentration of urine and, consequently, of the osmotic index ($P<0.05$; 0.02). Evidently, the cause of these changes in osmoregulatory function of the kidneys was a decline of hydrostatic pressure of a column of blood and, consequently, increase in intravascular volume, in view of the altered conditions of circulation of fluid between the aqueous spaces, as well as increased influx of blood to thoracic organs.

As a result of the circulatory changes, there was a 20% increase in rate of glomerular filtration on the first day ($P<0.05$) and, perhaps, there was decreased production of antidiuretic hormone, which led to a decrease ($P<0.02$) in reabsorption of osmotically free fluid ($P<0.02$). Evidently, there was also a decrease in secretion of mineralocorticoids at this time, as confirmed by increase in Na/K ratio ($P<0.05$). Decreased activity of the renin-angiotensin system and increased production of hypothetical natriuretic factor could also play some role in these changes [7].

After the increased elimination of fluid and electrolytes for the first 2 days of immersion, both groups of subjects presented a decrease and some stabilization of excretion thereof on the 3d-8th days (Figures 1 and 2). It should be noted that potassium excretion diminished only on the 3d and 4th days of immersion, and it progressively increased thereafter (see Figure 2).

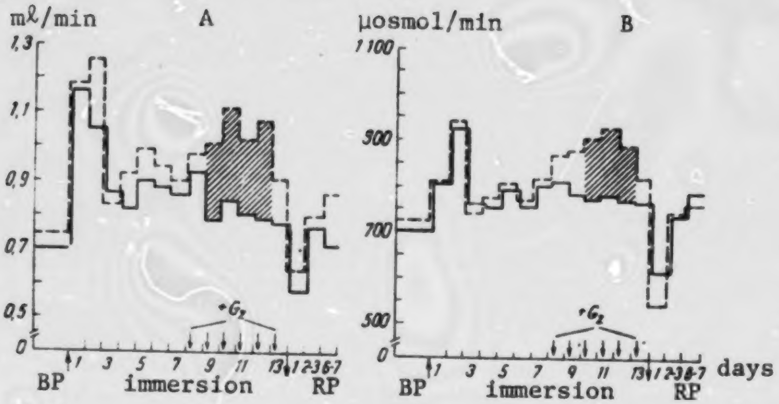


Figure 1. Rate of renal excretion of fluid (A) and osmotically active substances (B) at different stages of the study. Here and in Figure 2: solid line--1st group, dash line--2d group. The periods hashmarked refer to statistically significant differences between groups; BP--background period, RP--recovery period.

Thus, for the first 7 days of the study, the changes in renal function in both groups of subjects were essentially the same, and they were determined by duration of immersion.

Thereafter, a number of distinctions in renal function was demonstrated in the first group of subjects. Thus, on the 8th day of immersion, the rate of renal excretion of fluid, creatinine, sodium, potassium, calcium and osmotically active substances diminished in all subjects in the first group after the very first rotation on the centrifuge. However, as early as 4-8 h after the gravitational load, excretion of these substances again increased and level of daily elimination did not differ from that found in the second group (see Figures 1 and 2). Consequently, the first exposure to accelerations after 7 days of immersion elicited only a brief effect, with no substantial influence on daily balance of fluid and ions.

After subsequent rotation on the centrifuge, on the 9th-13th days of immersion, the changes in renal function were in the same direction as after the first rotation. However, there was longer retention of fluid and salts, as manifested by a decrease in mean daily rate of excretion of fluid and electrolytes in the first group of subjects, as compared to the progressively increasing elimination of these substances in the second group (see Figures 1 and 2). While elimination of potassium became stabilized at this time in the first group of subjects and virtually failed to differ from the level found on the preceding day, elimination of fluid, osmotically active substances and sodium even decreased and came close to base levels (see Figures 1 & 2). It should be noted that statistically significant differences between groups, with regard to rate of excretion of bivalent ions--calcium and magnesium--were demonstrable only on the last day of the study (see Figure 2).

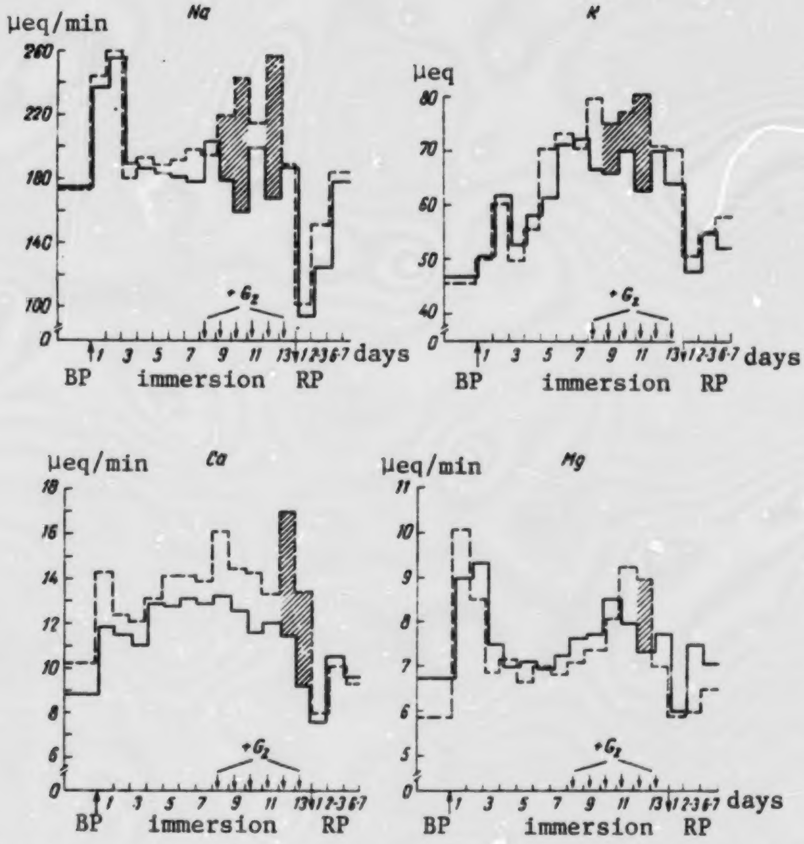


Figure 2. Rate of renal excretion of sodium, potassium, calcium and magnesium at different stages of the study

Periodic gravitational loads also affected ion content of blood serum (see Table). In the first group of subjects, there was no significant decrease in concentration of potassium in blood serum on the 10th and 12th days of immersion, as compared to the control. Calcium concentration increased in both groups of subjects on the 6th day of immersion. However, by the end of the observation period it presented a tendency toward increasing in the second group, whereas it remained on the same level in the first group. Exposure to accelerations did not affect magnesium content of blood serum; it increased on the last days of immersion in both groups of subjects. There was virtually no change in concentration of sodium and osmotically active substances at the tested times.

Typical redistribution of blood with decreased influx thereof to the heart, on the one hand, and increase in static load on the skeletomuscular system, on the other hand, are the most probable causes of changes in fluid-electrolyte metabolism and renal function with exposure to low levels of accelerations.

Concentration of electrolytes (in meq/ℓ) and osmolarity of blood serum (in mosmol/ℓ) in subjects during the experiment ($\bar{X}\pm m$)

Period	Day of exam.	Group of subjects	Concentration of				Osmolarity
			sodium	potass.	calcium	magnesium	
Background		1	143±1.6	4.5±0.15	4.8±0.14	1.70±0.09	292±2.9
		2	141±1,5	4,6±0.11	4,8±0.15	1,61±0.11	290±2,2
Immersion	3--4	1	150±1,2*	4.7±0.12	4,9±0,11	1,74±0.15	296±3,2
		2	147±1.4*	4,7±0.16	4.7±0.13	1.85±0.19	296±3,0
	6	1	147±2,1	4.5±0.12	5.3±0.16*	1.70±0.24	295±2,9
		2	145±2.5	4.7±0.17	5,3±0.10*	1.72±0.10	291±2,7
	10	1	142±0,9	4.3±0,18	5.3±0.19*	1.79±0.16	292±2.9
		2	144±2,7	4.1±0.11*	5.5±0.21*	1.79±0,09	297±3,8
	12	1	143±2,2	4.3±0.10**	5.3±0.20*	1.93±0,09*	290±3.4
		2	145±2,9	3.9±0.14**	5,6±0,17*	1.92±0,11*	295±3,9
Recovery	2—3	1	143±2,2	4.4±0.15	5,0±0,15	1,89±0,10	293±1,4
		2	147±2,3	4,2±0.11*	5.2±0.24	1.85±0.15	297±1,9
	7—8	1	142±2,2	4.6±0.17	4.9±0.18	1.72±0,16	292±1,5
		2	140±2,6	4.6±0.19	5.0±0.13	1.70±0,13	293±2,8
	11—12	1	142±1,8	4.4±0.25	4.8±0,21	1,68±0.17	291±3,3
		2	143±0.9	4.5±0,16	4.7±0.09	1,60±0,13	292±3,2

*Reliably significant changes, as compared to background.
**Reliably significant differences between groups.

With decrease in influx of blood to thoracic organs there is a decrease in impulsation from baroreceptors situated in the cavities of the heart, and as a result there is tonization of antidiuretic and antinatriuretic reflexes [8]. For this reason, there was increased reabsorption of osmotically free fluid ($P<0.05$) and decreased renal excretion of sodium ($P<0.02$) during exposure to accelerations. This was caused by the 36% decrease ($P<0.02$) in filtration load due to lesser glomerular filtration ($P<0.05$) and increased absorption of sodium in the renal tubules ($P<0.02$). Since the rate of glomerular filtration was restored to base levels within 1 h after rotation, the decreased excretion of sodium and fluid observed for the next 16-18 h was attributable to a change in transport thereof in tubules. This phenomenon may have been due to increased production of mineralocorticoids, as well as activation of the renin-angiotensin system in response to the typical circulatory change in the presence of increased gravity [9]. The rapid restoration of glomerular filtration warrants the belief that the observed changes in fluid-electrolyte metabolism can be attributed more to the distinctions of hormonal regulation of the kidneys than to circulatory changes in the kidneys. Evidently, the hemodynamic changes under the influence of accelerations were primary, triggering factors, while the hormonal ones were secondary and more static, for which reason the observed distinctions of osmoregulation and ionoregulation persisted for a rather long time.

The decreased rate of excretion in urine of the most important electrolytes of bone and muscle tissue (potassium, calcium and magnesium), as well as products of nitrogen metabolism (including urea and creatinine) on subsequent days in the first group of subjects, as compared to the second, can be attributed to the load on the skeletomuscular system during exposure to accelerations. It should be noted that a significant decrease in renal excretion of calcium and magnesium was noted only on the 11th-12th day of the study after 4-5-fold rotation on the centrifuge. Evidently, an increase in reabsorption of calcium and magnesium in renal tubules only occurs after long-term exposure to low levels of acceleration.

Thus, our studies demonstrated that it is possible, in principle to use periodic gravitational loads (+Gz) at low levels for preventive purposes and normalization of fluid-electrolyte metabolism and renal function during long-term immersion. The demonstrated decrease in excretion of fluid and salts in the first group of subjects prevented development of marked dehydration and negative electrolyte balance, which was largely involved in increasing resistance to +3 Gz accelerations after 13 days of immersion. A correlation was established between the changes in renal function and time of examination, as well as number of times the subjects were submitted to accelerations. A search for optimum mode of accelerations at different stages of studies, with due consideration of base state of hydroionic equilibrium and individual reaction of subjects to accelerations, as well as determination of the feasibility of combining this form of preventive treatment with other measures aimed at normalization of fluid-electrolyte metabolism should be the subject of future investigations.

BIBLIOGRAPHY

1. Balakhovskiy, I. S.; Bakhteyeva, V. T.; Beleda, R. V.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1972, pp 68-72.

2. Kakurin, L. I.; Grigor'yev, A. I.; and Kozyrevskaya, G. I. in "Mezhdunarodnyy astronavticheskiy kongress, 24-y. Tezisy" [International Congress of Astronautics, 24th, summaries of papers], Baku, 1973, pp 199-200.

3. Grigor'yev, A. I.; Dorokhova, B. R.; and Arzamazov, G. S. in "Nauchnaya konf. 'Fiziologicheskiye i klinicheskiye effekty lokal'nogo otritsatel'nogo davleniya.' Materialy" [Proceedings of Scientific Conference on "Physiological and Clinical Effects of Local Negative Pressure"], Moscow, 1976, pp 33-35.

4. Grigor'yev, A.I.; Paq, Z. P.; Koloskova, Yu. S.; et al. KOSMICHESKAYA BIOL., No 4, 1976, pp 55-59.

5. White, W. J., quoted by G. Wunger et al. "Gravity its a Biological Hypogravics [sic]. The Physiology of Inactivity and Weightlessness," New York, 1968, pp 55-62.

6. Shul'zhenko, Ye. B., and Vil'-Vil'yams, I. F. KOSMICHESKAYA BIOL., No 2, 1976, pp 82-84.

7. Epstein, M.; Katsikas, J. L.; and Duncan, D. C. CIRCULAT. RES., Vol 32, 1973, pp 228-236.

8. Gauer, O. H.; Henry, J. P.; and Behn, C. ANN. REV. PHYSIOL., Vol 32, 1970, pp 547-595.

9. Epstein, M.; Shubrooks, S. J.; Fishman, L. M.; et al. J. APPL. PHYSIOL., Vol 34, 1974, pp 340-344.

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CREATINURIA IN MAN DURING PROLONGED HYPOKINESIA

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[Article by S. A. Kamforina, submitted 17 Oct 77]

[English abstract from source]

A prolonged bed rest experiment of 94 days caused an increase in renal excretion of creatine during the first two months and a return to the pretest level during the third month. The bed rested test subjects who performed exercise showed a lower and delayed (by the 3rd month) increase in creatine excretion.

[Text] The question of creatine content in urine of healthy adults is debatable. There is the widespread opinion that normally no creatine is present in urine. It is believed that appearance thereof is related to an alimentary factor. However, a number of researchers have arrived at the conclusion that creatine is a constituent of urine, and they report significant fluctuations and individual differences in levels of excretion thereof [1-5]. Some authors have demonstrated creatinuria under hypokinetic conditions [6-8], while others failed to find a substantial increase in excretion of creatine [9].

Methods

We monitored daily excretion of creatine and creatinine (assayed by the method of A. D. Braun [10]) in 6 healthy males ranging in age from 20 to 23 years, who had been kept on bed rest for 94 days. The obtained data on creatinine excretion have been published previously [11, 12]. The subjects were divided into two groups, with three men in each. The first group maintained strict hypokinesia, and the second group performed in addition a set of physical exercises. Prior to the experiment, a control examination was conducted for 1 week with the usual motor activity. In order to make a comprehensive analysis of dynamic data, the findings were broken down into 8-10-day segments, each of which was compared to the control. Differences between groups were also determined within each time segment. The data were submitted to statistical processing according to criterion *t* of Student on a Minsk-22 computer.

In order to identify the chemical composition of the diet, we determined nitrogen content according to Kjeldahl, fat content according to Soxhlet, dry residue content by the method of desiccation to a constant weight at temperatures of 100-105°C, ash by the ashing method and carbohydrates by calculation according to difference. Food intake was measured throughout the period of the study. The data pertaining to alimentary status used here were obtained with the help of I. M. Buznik, O. A. Goryacheva [deceased] and T. V. Egle.

Results and Discussion

Protein intake by the first group of subjects decreased from 128.7±1.5 g to 118.4 3.1 g ($P<0.01$) by the 49th day and to 99.8±4.9 g at the end of the experiment. In the second group, this index rose from 130.0±1.4 g to 141.2±2.9 g ($P<0.01$) by the 3d week, but returned to the control level between the 77th and 94th days. Fat intake by the first group of subjects dropped to 70.4±3.7 g toward the end of the hypokinetic period, versus 81.5±3.5 g in the control period ($P<0.05$). In the second group, this index was reliably higher than in the first group from the 41st day on, but it was unreliable as compared to the control period ($P<0.05$). Carbohydrate intake by the first group dropped from 322±5 g to 283±9 g ($P<0.001$) by the end of the experiment, whereas it increased to 337±4 g in the second group, the base level being 323±5 g ($P<0.05$). In the first group, the caloric value of consumed food was reliably lower between the 25th and 94th days of hypokinesia than in the second group; in the control period this index constituted 2607±22 and 2610±21 kcal, respectively. In the first group, food intake began to diminish on the 41st day and constituted 2226±65 kcal by the end of the hypokinetic period ($P<0.001$); in the second group it began to increase on the 17th day, the maximum constituting 2819±25 kcal ($P<0.001$).

One subject in the first group lost 1.4 kg and one in the second group gained 1.2 kg; weight changes were less marked in the others. Consequently, it may be assumed that nutrition was adequate.

The Table lists data on excretion of creatine in urine. In the first group, creatine excretion began to increase by the 3d week, it reached a maximum by the end of the 2d month and then gradually dropped to the control period level. In the second group, there was less marked increase in excretion of creatine, it appeared later, by the start of the 3d month, and persisted to the end of the experiment. The level of creatine excretion between the 33d and 67th day of bed rest was reliably higher in the first group than in the second. The changes in creatine excretion in different subjects within groups were similar, but the extent varied.

There was significant fluctuation of creatine content of urine, and the coefficient of variation constituted 24-63% in the control period. During the period of bed rest, the daily fluctuations of excretion were more marked and the coefficient of variation was in the range of 14-111.1%. In the daytime (from 0900 to 2100 hours), 50.6-73.7% of 24-h amount of creatine was excreted. When scaled to 1 kg body weight, 1 g total urine nitrogen and 1 g creatinine, the general nature of changes in creatine excretion remained unchanged, but there were differences in degree of their reliability. These changes were more marked when scaled to 1 g total nitrogen of urine. In the first group, the maximum increase in creatine excretion by the end of the 2d month of hypokinesia constituted 1.82±0.17 mg/kg body weight and 8.4±0.8 mg/g total nitrogen of urine, versus 1.20±0.11 and 4.9±0.4 mg in the control period (P<0.01 and <0.001). In the second group, higher levels were found in the last week of hypokinesia: 1.52±0.12 mg/kg and 5.9±0.5 mg/g, versus 1.04±0.10 mg/kg and 4.2±0.4 mg/g in the control period (P<0.01 and <0.05). In the control period, creatine excretion constituted 5.73±0.84-6.79±1.02% in relation to creatinine in 5 subjects and 10.87±1.08% in one, which corresponded to group means of 7.80±0.73 and 6.32±0.61%. At the height of excretion toward the end of the 2d month of hypokinesia, the indices of creatine excretion constituted 10.94±0.99% of creatinine excretion in the first group (P<0.05), and it dropped to 7.3±0.83% at the end of the bed rest period. In the second group, 7.71±0.60% creatine was excreted at the end of the study (the increase was unreliable, as compared to the control period).

Excretion of creatine in urine, mg/day

Period	Group				$P_{1,2}$
	1		2		
	n	$\bar{x} \pm S_{\bar{x}}$	n	$\bar{x} \pm S_{\bar{x}}$	
Control	21	88±7,4	21	73±7,5	>0,05
Hypokinesia:					
1—8-th days	24	94±9,3	24	66±8,3	<0,05
9—16 "	24	100±14,9	24	73±6,5	>0.05
17—24 "	24	126±11,5**	24	96±10.6	>0,05
25—32 "	24	115±14,0	24	92±8,7	>0,05
33—40 "	24	118±9,9*	24	80±6,8	<0,01
41—49 "	27	115±11,0	26	80±9.6	<0,05
50—59 "	30	132±11,6**	30	99±9.6*	<0,05
60—67 "	24	119±9,6*	24	90±8.1	<0,05
68—76 "	27	107±10,4	27	97±7,2*	>0,05
77—85 "	27	93±7,3	27	94±7,4	>0.05
86—94 "	27	85±10,0	27	105±8,4**	>0,05

*P<0.05
**P<0.01, as compared to control

$P_{1,2}$) reliability of differences between groups

A partial correlation was demonstrated between excreted creatine and total urine nitrogen (r = 0.53) and creatinine (r = 0.52), with a very slight correlation to diuresis (r = 0.25).

We cannot consider the cause of creatinuria to have been definitively determined; however, some opinions on this score can be voiced on the basis of a number of studies. The opinion is held that appearance of creatinuria is related to impairment of carbohydrate metabolism or inadequate carbohydrate intake with food [13]. In our studies, higher levels of creatinuria were observed in the first group, and there was more significant decrease in carbohydrate intake in this group; however, a greater decrease in carbohydrate intake was noted in the last weeks of hypokinesia, while the higher creatine level was noted in the 2d month. Thus, we failed to demonstrate any correlation between developing creatinuria and level of carbohydrate intake.

Studies using labeled atoms [14, 15] established that the increase in creatine content of urine in the presence of muscular dystrophy is not due to release of muscular creatine as a result of dissociation, but inability of muscles to utilized synthesized creatine. Creatinuria in the case of immobilization is also attributed to diminished muscular capacity to utilize creatine [8]. The increased creatine excretion demonstrated in our study can apparently be attributed to diminished creatine requirement due to forced restriction of muscular activity. Creatinuria, which appears in the first few weeks, increases during the first 2 months of strict hypokinesia, and this is perhaps due to the diminished capacity of muscles to utilize creatine as a result of development of atrophic processes, which lead to reduction of ATP, creatine phosphate and creatine content of muscles [16]. Under hypokinetic conditions, there is diminished function of enzyme systems and phosphorulation level [17], so that it may be assumed that there is a limitation on processes of production of creatine phosphate. As the body adapts to hypokinesia, there is apparently also decrease in creatine synthesis, conforming with the decreased requirement thereof, and excretion in urine diminishes.

As shown by the studies, in the presence of hypokinesia associated with physical exercise, no decrease in creatine excretion is observed. Probably the exercises are instrumental in retention of muscular capacity to utilize creatine and maintain synthesis thereof on a higher level.

On the basis of the studies, it can be concluded that increased creatine excretion does occur during prolonged, forced hypokinesia, but only for the first 2 months. Starting with the 3d month of bed rest, creatine excretion in urine gradually drops to the base level. An additional physical load attenuates creatinuria and postpones the time of increase therein, thereby aiding in preservation of the energy potential of muscles, which is important to the body.

BIBLIOGRAPHY

1. Ahlert, G.; Bruschke, G.; Dietze, F.; et al. Z. ALTERNSFORSCH., Vol 20, 1967, pp 113-118.

2. Albanese, A. A., and Wangerin, D. M. SCIENCE, Vol 100, 1944, pp 58-60.

3. Beard, H. H. "Creatine and Creatinine Metabolism," Brooklyn, 1943.

4. Wang, E. ACTA MED. SCAND., Suppl 105, 1939.

5. Wilder, V., and Morgulis, S. ARCH. BIOCHEM., Vol 42, 1953, pp 69-71.

6. Syzrantsev, Yu. K. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 7, 1967, pp 342-347.

7. Fedorov, I. V., and Grishanina, L. A. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1967, pp 43-48.

8. Heilskov, N. C. S., and Schonheyder, F. ACTA MED. SCAND., Vol 151, 1955, pp 51-56.

9. Whedon, G. D.; Deitrick, J. E.; and Shorr, E. AM. J. MED., Vol 6, 1949, pp 684-711.

10. Braund, A. D. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 10, 1954, pp 73-76.

11. Buznik, I. M., and Kamforina, S. A. KOSMICHESKAYA BIOLB, No 4, 1973, pp 60-64.

12. Kamforina, S. A. "Creatine and Creatinine Metabolism During Long-Term Hypokinesia," author abstract of candidatorial dissertation, Leningrad, 1975.

13. Tolkachevskaya, N. F. "Development of Metabolic Processes in Infants up to One Year Old," Moscow, 2d edition, 1960.

14. Benedict, J.; Kalinsky, H.; Scaroone, L.; et al. J. CLIN. INVEST., Vol 34, 1955, pp 141-145.

15. Dinning, G. S., and Fitch, C. D. PROC. SOC. EXP. BIOL. (New York), Vol 97, 1958, pp 109-111.

16. Ferdman, D. L.; Mestechkina, A. Ya.; and Semenov, N. V. DOKL. AN SSSR [Reports of the USSR Academy of Sciences], Vol 75, No 5, 1950, pp 757-759.

17. Kovalenko, Ye. A. KOSMICHESKAYA BIOL., No 1, 1976, pp 3-15.

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CHANGES IN THE NEUROMOTOR SYSTEM DURING 45 DAYS OF HYPOKINESIA

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[Article by Ye. A. Shaposhnikov, P. I. Sidorov and A. I. Kolomenskiy, submitted 25 Jan 77]

[English abstract from source]

Neurological and electromyographic examinations of 12 test subjects during a 45-day bed rest study were carried out. Symptoms indicating changes in the suprasegmentary innervation were noted. Shortening of the duration of potentials was shown by needle electromyography. A decline in the threshold of H-reflex and a change in the frequency parameters of EMG were seen. These data suggest a change in the functional state of the central and peripheral motor neuron during prolonged hypokinesia. Prophylactic efficiency of muscle electrostimulation is discussed.

[Text] The problem of functional state of various organs and systems in the case of prolonged restriction of motor activity has acquired general physiological, clinical and applied significance in the last few years. This is related to the fact that a number of special investigations demonstrated the adverse effect of hypokinesia on many physiological processes in the body [1-3].

There are data indicating that prolonged (over 10-14 days) restriction of motor activity in the absence of a load along the longitudinal axis of the body leads to development of various changes in the motor area [3, 4]. In these studies, attention was devoted mainly to such clinical manifestations as diffuse hypotonia and hypotrophy of so-called antigravity muscles (most muscles of the back, some muscles of the pelvic girdle and legs), diminished turgor of muscle tissue, of static and dynamic endurance. Of great interest are morphological, biochemical and cytochemical studies [5, 6] of skeletal muscles under hypokinetic conditions, which indicate that an atrophic process develops in them. Changes in excitability of the peripheral element of the neuromotor system (muscles) have been demonstrated in neurophysiological studies [7], while electromyographic studies of man, using a superficial lead [8, 9] demonstrated changes in frequency indices and, in a number of cases, amplitude parameters as well. At the same time, no works have yet been published about the functional state of neurophysiological systems that regulate the locomotor act (synaptic system, spinal structures). Data are needed in this area in order to develop pathogenetically substantiated therapeutic and preventive measures.

Methods

The objective of this study, which was conducted under clinical conditions on 12 healthy volunteer subjects who spent 45 days on strict bed rest (head tilted down at an angle of -6°), was to compare the results of complex neurophysiological and clinical examination of the motor system. Electric stimulation of the muscles of the legs, abdomen and back, using the Tonus-2 instrument, following the program proposed by M. A. Cherepakhin [10], was delivered to 8 subjects for preventive purposes. These individuals were divided into two groups (four in each), differing in method of delivering electrostimulation. The first method of electrostimulation (20 electrodes) referred to force lines along the surface (along muscles), with the second method (12 electrodes) the force lines traversed the entire thickness of the muscles, which enabled us to stimulate many muscles with one pair of electrodes. Thus, the subjects were divided into three groups (of four men each): the first consisted of individuals who did not undergo electric stimulation (control); the second and third groups consisted of subjects submitted to electrostimulation by the first and second methods, respectively.

Systematic examination of neurological status (every 7-10 days) included a particularly thorough examination of the neuromotor system and, in particular, reflexes. The subjects kept a diary containing a special questionnaire-scale, in which they entered data concerning the state of the nervous system and organism as a whole. The subjectively perceived neurological symptoms were graded by the subjects on a 3-point scale (0--no disturbances, 1--mild ones, 2--moderate, 3--severe). This method made it possible to quantitatively determine the intensity and dynamics of subjective symptoms of hypokinesia and to make a more accurate evaluation of the preventive efficacy of electrostimulation.

Electrophysiological examination of muscles, particularly antigravity ones, was made prior to the experiment, during hypokinesia (15th-20th and 45th days) and 10-15 days after the bed rest. We performed "global" (superficial) electromyography of extensors and flexors of the feet and hands, and "local" (using needle electrodes) recording of action potentials of individual motor units (MU) in the tibial muscle. Conventional functional tests were used: synergistic reactions, maximum voluntary contraction and fatigue test. The fatigue test involved maximum tension of the tested muscle for as long as possible. The time of onset of fatigue (while monitoring the force of the maximum contraction according to mean EMG frequency) was determined according to appearance of specific subjective sensations in the muscle, against the background of typical changes in frequency parameters on the EMG.

Bioelectric potentials were recorded on a Disa (Denmark) three-channel electromyograph. For the global tracing, we used standard disk electrodes and for local registration of MU action potentials we used concentric bipolar type 13K62 electrodes. Mean duration of MU action potentials [11, 12] was calculated on the basis of 1000-1200 readings in each group. A standard method [13] was used to test the H-reflex threshold, latency period and ratio between H and M responses. Stimulation was delivered by a type 14E01 stimulator.

Qualitative analysis of global EMG's was made in accordance with the conventional classification [12]; quantitative analysis of frequency and amplitude included evaluation of probabilistic frequency structure of the EMG [14]. Mean frequency of EMG spectra in the endurance [fatigue] test was determined on the basis of 90-100 measurements using ChZ-8 and MIAN-1 frequency counters with averaging time of 1 to 4 s. Part of the EMG was processed on a computer.

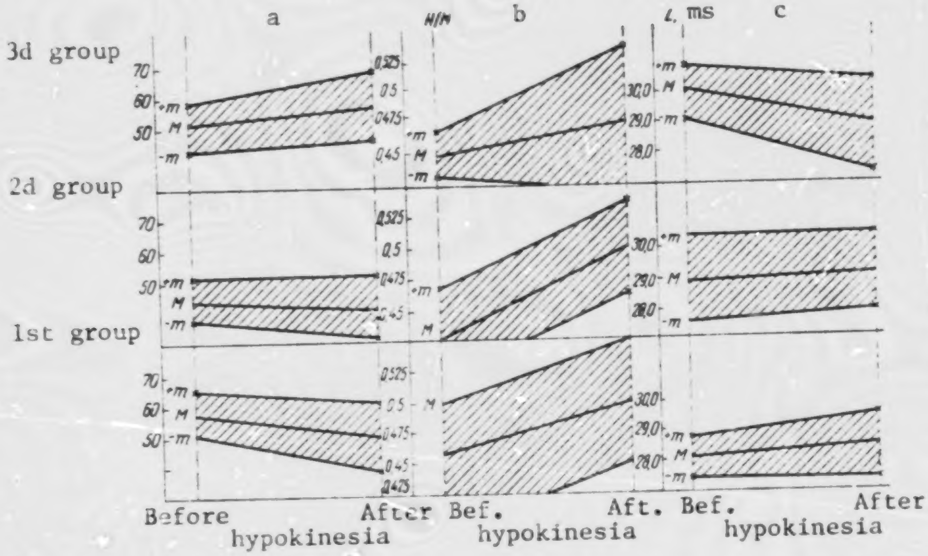
In view of the small size of the groups, the statistical parameters were obtained by the formulas for sample coefficients. Reliability was determined according to Student.

Results and Discussion

Changes, both objective and subjective, appeared in muscles (weight loss, diminished turgor) and were more marked in leg muscles after 10-15 days of hypokinesia. At the same time, all groups of subjects presented changes referable to reflexes: nonuniform and assymetrical tendon reflexes, against the background of a general tendency toward activation thereof, diminished skin and, in particular, abdominal reflexes, appearance of oral automatism reflexes and pathological signs in the feet. These changes are indicative of decreased descending regulatory influences from suprasegmental and, in particular, pyramidal structures.

We should discuss in particular the syndrome of motor disorders observed in all subjects after discontinuing bedrest. There was increased fatigability of muscles (mainly antigravity ones) when walking for a long time, sensation of clumsiness, rigidity [heaviness] of the legs and other discoordination phenomena. There was instability in Romberg's sensitized position, rocking when walking, particularly in a straight line, etc. These symptoms were observed on the first 2-3 days of the recovery period (grade of 1-2 according to self-appraisal by the subjects, without clearcut difference between groups). The "neuromyalgic syndrome" was more persistent; it appeared 12-18 h after returning to ordinary motor activity. It was manifested by tenderness of muscles, which made walking difficult for some subjects. The most severe pain was referable to antigravity muscles, ligament system of the lower legs and particularly the feet. The pain appeared not only when walking, but with negligible movement during the first 3 posthypokinesia days; palpation of the muscles aggravated the pain. The pain syndrome was observed for 7-10 days, lasting 2-3 days longer in the first group than in the others. According to the subjects' self-appraisal, the intensity of pain was rated at up to 2-3, whereas it did not exceed 1-2 in most cases for subjects in the second and third groups.

There were no qualitative changes on the EMG of all subjects, either before or after hypokinesia, and it corresponded to the first type in the classification of Yu. S. Yusevich [12]. This is indicative of absence of pathological changes in motoneurons of the anterior cornua. As for the H-reflex (see Figure), its parameters were altered by hypokinesia, even against the background of muscular stimulation. In the first group, there was a tendency toward decline of thresholds of excitability of the H-reflex, whereas in the groups where electrostimulation of muscles was included there was virtually no change in excitability threshold. The ratio between H and M responses increased somewhat in all groups, and the tendency toward increase was the most marked in the second group. The changes in latency time (L) of the H-reflex were unreliable.



EMG parameters before and after hypokinesia, evaluated by the method of stimulating electromyography

a) threshold of H-reflex (V)
b) ratio between H and M responses
c) latency time of H-reflex (ms)

The demonstrated changes (which are particularly distinct in the control group) are indicative of increased reflex excitability of the motoneuron pool. We cannot rule out the possibility that this process develops secondarily, in view of attenuation of descending influences from the reticulohypothalamic system, which expresses its influence via the reticulospinal routes. The change in functional state of the hypothalamoreticular complex under the influence of drastic decrease in afferent impulsation that activates it (primarily proprioceptive impulsation) in the presence of hypokinesia is a known phenomenon [15, 16].

The study of functional state of muscular MU using needle recording of the EMG revealed a decrease in duration of action potential of individual MU in the tibial muscle of subjects in the first and third groups. In the light of current conceptions [13, 17, 18], this could be indicative of a decrease in number of actively functioning fibers in the MU zone, which is perhaps related to a change in synaptic structures in muscles in the case of prolonged inactivity. In the second group of subjects, there was no change in duration of MU potentials and, in our opinion, this is indicative of the preventive effect of electrostimulation with a maximum number of electrodes, which prevents development of functional "elimination" of muscle fibers.

The preventive effect of electrostimulation was confirmed by the results of examining the frequency index of the EMG in the endurance test. A decline of mean EMG frequency for all tested muscles was inherent in the first group of subjects. In the second group, a tendency toward decrease in mean EMG frequency was noted only in muscles not submitted to electrostimulation (hands). In the third group (minimum number of electrodes), the EMG frequency index did not drop only in the gastrocnemius, which was stimulated directly.

It should be noted that we also observed a decrease in time of holding an active maximum contraction and faster appearance of subjective and objective signs of fatigue (by 30% in the tibial muscle, for example), as compared to the background period, in subjects of all groups. The decline of mean EMG frequencies with prolonged hypokinesia could, as indicated by the literautre [19, 20], also be related to a decrease in number of actively stimulated myoneural endings in the region of an individual motor unit, as a result of the atrophic process, and change in function of synaptic structures. This hypothesis appears quite plausible if we consider the morphological data concerning a link between an atrophic process in hypokinetic muscles and proliferation of perivascular connective tissue in them [20]. Electrostimulation, which activated by directly and reflexly local metabolism in muscle tissue, could prevent these changes to some extent.

A comparison of the results of electrophysiological and direct neurological studies revealed that the most marked clinical symptoms (graded as 2-3) and EMG changes coincided in 86% of the cases. This could be interpreted as a sign of informativeness of the system of evaluating clinical phenomena on a point scale and the desirability of clinicophysiological comparisons, which make it possible to determine more fully (both quantitatively and qualitatively) the nature and intensity of a process.

The results of these studies are indicative of a complex, combined reaction to hypokinesia of neurophysiological systems that implement proper reflex-motor activity on different levels of the neuromotor system.

Electrostimulation of muscles did not have a clearcut beneficial effect on indices of functional state of the central elements of the neuromotor system (reflexes, coordination). At the same time, some beneficial effect was observed with respect to some symptoms attributable to the reaction of peripheral elements of the neuromotor system to hypokinesia. Clinically, this was manifested by a significantly milder postkinetic pain syndrome referable to muscles of the feet and lower legs in subjects submitted to electrostimulation (particularly the second group).

The electrophysiological studies demonstrated the preventive effect of electrostimulation, as manifested by retention of indices of excitability of segmental motoneurons (H-reflex) and absence of changes in frequency characteristics of the EMG. The duration of action potentials of individual MU did not change only in the second group of subjects, and this is apparently attributable to the stronger effect on muscle tissue of electrostimulation using a maximum number of electrodes.

BIBLIOGRAPHY

1. Kraus, H., and Raab, W. "Hypokinetic Disease. Diseases Produced by Lack of Exercise," Springfiled, 1961.

2. Kakurin, L. I. "Effect of Limited Muscular Activity on Man," doctoral dissertation, Moscow, 1968.

3. Cherepakhin, M. A. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1968, pp 43-47.

4. Panov, A. G.; Lobzin, V. S.; and Mikhaylenko, A. A. ZH. NEVROPATOL. I PSIKHIATR. [Journal of Neuropathology and Psychiatry], No 4, 1973, pp 506-511.

5. Portugalov, V. V.; Il'ina-Kakuyeva, Ye. I.; Starostin, I. D.; et al. ARKH. ANAT. [Archives of Anatomy], No 11, 1971, pp 82-91.

6. Gayevskaya, M. S.; Kurkina, L. M.; Kolchina, Ye. V.; et al. in "Biofizicheskiye osnovy patologicheskogo sostoyaniya mushts i energeticheskove obespecheniye sokratitel'nogo apparata" [Biophysical Bases of Muscular Pathology and Delivery of Energy to the Contractile System], Tbilisi, 1973, pp 36-38.

7. Oganov, V. S., and Potapov, A. N. KOSMICHESKAYA BIOL., No 2, 1973, pp 22-26.

8. Petukhov, V. N., and Purakhin, Yu. I. KOSMICHESKAYA BIOL., No 2, 1971, pp 64-68.

9. Tishler, V. A., and Safonov, V. I. in "Kosmicheskaya biologiya i aviakosmicheskaya meditsina" [Space Biology and Aerospace Medicine], Moscow--Kaluga, Vol 2, 1972, pp 152-154.

10. Cherepakhin, M. A.; Kakurin, L. I.; Il'ina-Kakuyeva, Ye. I.; et al. KOSMICHESKAYA BIOL., No 2, 1977, pp 67-70.

11. Person, R. S. "Electromyography in Studies of Man," Moscow, 1969.

12. Yusevich, Yu. S. "Essays on Clinical Electromyography," Moscow, 1972.

13. Baykushev, St.; Manovich, Z. Kh.; and Novikova, V. P. "Stimulating Electromyography and Electroneurography in Clinical Practice Referable to Neurological Diseases," Moscow, 1974.

14. Kolomenskiy, A. I., and Sidorov, P. I. in "Voprosy klinicheskoy elektromiografii" [Problems of Clinical Electromyography], Vil'nyus, 1973, pp 64-65.

15. Mogendovich, M. R., and Temkin, I. B. "The Analyzers and Viscera," Moscow, 1971.

16. Parin, V. V., and Fedorov, B. M. in "Aviatsionnaya i kosmicheskaya meditsina" [Aviation and Space Medicine], Moscow, Vol 2, 1969, pp 116-118.

17. Person, R. S. in "Paraklinicheskiye metody issledovaniya v nevrologicheskoy klinike" [Paraclinical Examination Methods in Neurological Practice], Moscow, Vyp 1, 1969, pp 159-167.

18. Markov, D. A. "Fundamentals of Pathogenetic Therapy of Diseases of the Nervous System," Minsk, 1964.

19. Gausmanova-Petrusevich, I. "Diseases of the Muscles," Warsaw, 1971.

20. Portugalov, V. V.; Il'ina-Kakuyeva, Ye. I.; Rokhlenko, K. D.; et al. in "Aviatsionnaya i kosmicheskaya meditsina," Moscow, Vol 2, 1969, pp 163-167.

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085.844-039.71

ELECTROSTIMULATION OF MUSCLES FOR THE PREVENTION OF NEUROMUSCULAR DISORDERS DURING 45-DAY ANTIORTHOSTATIC HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 40-44

[Article by V. S. Georgiyevskiy, Ye. A. Il'inskaya, V. I. Matveyev, V. M. Mikhaylov and V. I. Pervushin, submitted 16 Jan 78]

[English abstract from source]

Healthy test subjects exposed to a 45-day head-down tilting (−6.5°) showed a decline of the tone and strength of certain muscle groups, a decrease of leg circumference, a deterioration of the walking pattern, and a reduction of exercise tolerance (provocative tests with bicycle ergometry pedalling at a moderate and maximum rate). Electrostimulation of muscles applied by the Tonus-2 equipment for 30 min twice a day, 6 days a week helped to reduce the level of hypokinesia-induced disorders.

[Text] This work is part of a series of studies pursued for the purpose of theoretical substantiation and evaluation of the efficacy of various preventive measures to be used during long-term space flights. In our previous report [1], we submitted data on the effect of various methods of muscular electrostimulation during prolonged bed rest on man's orthostatic stability. In this report, we submit data on the effect of myoelectrostimulation on the neuromuscular system and physical fitness.

Methods

This study was conducted on 12 healthy male volunteers (3 groups of 4 men) ranging in age from 22 to 35 years who remained for 45 days in a state of antiorthostatic [head tilted down] hypokinesia (AOH) at an angle of -6 5°. The subjects in the first and second groups were submitted to stimulation of anterior and posterior muscles of the legs and thighs, as well as back and abdomen, using a Tonus-2 instrument, during the hypokinetic period. Stimulation was delivered 6 times a week, twice a day, for 30 min at a time. In the first group, electrostimulation was delivered using 20 electrodes, stimulating each of the above muscle groups with a separate pair of electrodes. In the second group, 12 electrodes were used to stimulate the same muscle groups. The number of electrodes was reduced due to a change in system of applying them and some updating thereof: the muscles of the leg and posterior femoral group were stimulated with the same pair of electrodes, instead of three.

We measured the perimeters of the limbs, performed tonometry of the muscles according to Sirman, ichnography, body and hand dynamometry for complex evaluation of the state of the neuromuscular system and physical fitness. In addition, we used functional tests with physical loads. We determined the maximum time for holding a standard weight attached to the feet with the legs straight and elevated (20 cm) in supine position as an index of static endurance. The reaction to a measured physical load was examined by means of a functional test on a bicycle ergometer in seated position, with force of performed work of 450 kgf/min for 10 min and pedaling rate of 60-70 per min. Endurance of step-by-step increasing load was evaluated by means of a test on the bicycle ergometer. The subjects began the test at a force of 600 kgf/min, which was then increased by 200 kgf/min each minute. The test was continued until the subject was completely tired. During the functional tests with physical loads on the bicycle ergometer, we took a continuous record of heart rate from the EKG and discrete measurement of arterial pressure before and after the test. A biopsy of the solar muscle was taken from all subjects prior to the period of bed rest and 15 days before the end of this period.

Results and Discussion

General condition and endurance of 45-day AOH were better among individuals whose muscles were submitted to electrostimulation. As a rule, the sessions gave the subjects pleasure and were perceived as a pleasant treatment, which alleviated their confinement to strict bed rest. The sensations following electrostimulation resembled those experienced after mild physical work or massage of the muscles.

Toward the end of the period of AOH, all subjects presented a reduction in perimeters of the lower limbs and decreased muscle tone in the legs and thighs, the tendency toward change being less significant in the first and second groups than in the control. Thus, on the 40th day, the perimeters of the crus diminished (on the average) by 20.7, 25.2 and 51.0 mm in subjects of the first, second and third groups, respectively, and those of the thigh by 5.0, 24.3 and 31.0 mm. The difference between mean changes in perimeters, as compared to the control group, was statistically significant ($P<0.05$). There was 11.5, 7.4 and 21.2% decrease in firmness of the tibial muscle and 8.1, 10.8 and 10.1% decrease in firmness of femoral muscles. There was virtually no change in tonus and perimeters of the arm in all groups of subjects.

Immediately after AOH, the test with ichnography revealed unstable walking in all subjects, the most marked changes being noted in the control group. The latter deviated more from the specified straight line, took shorter steps, spreading their legs far apart. In the first and second groups the average deviation of the body from the straight line constituted 47 mm (the difference between these groups is insignificant), and in the control group it was 88 mm ($P<0.05$). Accordingly, the length of a step constituted 680 mm and 540 mm ($P<0.05$), while the distance between the right and left foot when walking constituted 41 and 53 mm ($P<0.05$). Interestingly enough, in most cases, the first deviations from the axial line were in the same direction as the side on which the subjects spent most of the time during the period of bed rest.

"Upright strength"[? power for motor coordination] diminished in two subjects in the first group, three in the second and all four in the control group. The mean decline constituted 8.7, 19.1 and 20.6% in these groups, respectively. There was insignificant change in hand dynamometry in all groups of subjects. Static endurance increased by an average of 52 and 36% in the first and second groups of subjects, respectively, under the influence of a course of electrostimulation of muscles, whereas in the third group it dropped by 9.9%. The difference between mean values was significant, as compared to the results for the control group ($P<0.05$).

The tested with a measured physical load, which was performed 1 day after AOH, elicited a more marked cardiovascular reaction in all groups, the most marked changes being noted in the control group; they were less marked in the second group and the least marked in the first (see Table). The background measurements taken before the physical exercise already showed that the heart rate was 30-32/min higher than under analogous conditions before the start of AOH in the first and second groups, and 56/min higher in the third ($P<0.05$). Pulse pressure decreased by 13, 14 and 15 mm Hg, respectively. These changes could have been largely due to decrease in orthostatic stability of the subjects [1], since the test on the bicycle ergometer was performed in seated position. During exercise following AOH, the highest heart rate was recorded on subjects in the third group. Thus, immediately after pedaling, the heart rate was higher in the first and second groups of subjects than before AOH, by an average of 43-44/min, and in the control group it was 60/min higher. Pulse pressure dropped by 16, 26 and 31 mm Hg, respectively. This change in reaction of the cardiovascular system to the same physical exercise is indicative of decreased economy of muscular activity.

The test involving a step-by-step increase in physical load after AOH showed a decrease in physical fitness of all subjects, and it was somewhat more marked in the control group. Thus, the volume of work performed decreased by an average of 30.3, 34.8 and 38.8% in the first, second and third groups, respectively. In spite of the decreased volume of work, the heart rate was considerably higher at the time the exercise stopped than in the background studies, which is indicative of worsening of the cardiovascular reaction to the physical load.

Heart rate and arterial pressure during tests with measured physical load (450 kgf/min, 10 min) before (I), on the 1st day (II) and 10th day (III) after termination of AOH

Group	Parameters	Stage	Before load	After load, min			
				1	3	5	10
1	Heart rate, per min	I	75±5.35	86±7,75	80±6,25	78±5,47	73±2,87
		II	105±5,34**	129±7,56*	118±6,98**	113±5,87**	104±3,13**
		III	87±5,52*	101±5,34	89±6,12	88±5,98	85±6,86
	Systolic pressure, mm Hg	I	122±3,71	139±3,75	131±6,57	125±5,70	120±3,53
		II	122±0,64	135±3,53	126±2,39	130±4,56	124±7,18
		III	117±2,12	143±1,47	121±3,75	114±3,75	116±3,75
	Diastolic pressure, mm Hg	I	84±3,02	89±7,46	85±2,04	79±5.15	75±2,88
		II	93±3,35*	101±3,75	98±4,34**	99±6,25**	91±6,57
		III	85±2,78	96±3,75	84±2,39	84±4,27	84±3,75
	Pulse pressure, mm Hg	I	41±3,18	50±6,12	46±5,54	46±5,54	45±2,04
		II	28±3,53**	34±6,26	29±3,75**	31±4,27*	31±4,27**
		III	31±2,27**	46±4,27	38±3,24	33±3,24**	35±5,40 *
2	Heart rate, per min	I	80±3,84	90±2,39	90±2,41	83±2,91	82±2,93
		II	112±8,58**	134±6,47**	118±6,63**	115±6,61**	117±6,98**
		III	92±4,52*	100±5,13	96±6,52	91±5,87	88±5,66
	Systolic pressure, mm Hg	I	121±2,32	140±2,04	128±2,51	116±5,91	113±4,34
		II	112±3,93**	124±7,18*	119±3,14*	110±2,88	106±1,25
		III	114±7.44	128±2,51*	123±7,78	119±4,27	113±6,62
	Diastolic pressure, mm Hg	I	79±2,54	78±4,57	76±3,75	69±4,27	69±1,25
		II	85±2,85	85±4,08	83±1,47	78±1,47*	78±1,47**
		III	78±0,64	74±5.54	75±5.00	78±4,79	76±5,54
	Pulse pressure, mm Hg	I	44±0,91	65±2,04	51±5.15	48±4,79	44±4,73
		II	30±5,15**	39±9,65**	34±3,75**	33±3,24**	29±1,25**
		III	35±3,57**	54±4,27*	48±6,62	41±3,14	36±4,73
3	Heart rate/ per min	I	75±1,85	96±14,31	88±10.79	90±10,32	85±8,90
		II	131±7,03**	156±8,78**	145±8,45**	139±13.81**	137±12,84**
		III	80±3,14	104±5.90	85±7,54	84±5,89	81±6,14
	Systolic pressure, mm Hg	I	113±4,95	137±11,61	132±7,30	124±5.38	117±8,97
		II	104±5,45	113±4,79	110±2,01**	109±4,27*	109±2,39
		III	108±2,95	130±0	111±5,54*	104±2,39**	105±0
	Diastolic pressure, mm Hg	I	80±1,60	78±4,81	80±3.30	85±3,04	79±3,14
		II	86±6,15	85±5,40	88±4,79	84±3,75	83±3,24
		III	79±1,78	81±5,15	76±5,15	74±1,22**	74±2,39
	Pulse pressure, mm Hg	I	34±3,45	59±13,2	52±9,65	39±8,26	38±8,98
		II	19±2,48**	28±4,34*	25±4,56**	26±2,39	26±2,39
		III	30±4,49	50±5,77	35±4,56	30±2,04	31±2,39

*Difference between levels in given period and period I is significant with P<0.1.

**Same as above, with P<0.05.

By the 10th day of the recovery period, there was a distinct tendency toward normalization of most tested parameters, and this was more marked in the first group; there was an appreciable difference from base levels in the parameters recorded for the control group.

The obtained data indicate that the course of electrostimulation of muscles has some preventive effect on certain parameters of the neuromuscular system and physical efficiency of man during long-term bed rest. The most marked protective effect of electrostimulation was obtained in the first group of subjects; it was less distinct in the second group; however, the differences between these groups were found to be insignificant, according to a number of parameters (perimeter of lower leg, muscular tonus, ichnography, static endurance, tested with measured and stepped-up load on bicycle ergometer).

On the whole, apparently activation of the central nervous system and metabolic processes on the order of motor-visceral reflexes [2, 3] is the positive element in the effect of electrostimulation on the human body. No doubt, the positive effect of electromyostimulation is manifested primarily by prevention of development of atrophy of skeletal muscles. In experimental studies on animals, a beneficial effect of electrostimulation against the background of hypokinesia was noted in 30% of the cases [4]. Either no destructive and metabolic changes in muscle fibers developed, or else they were quite minimal. In this study, biopsy of the gastrocnemius of subjects in the first and second groups merely showed some development of atrophic processes, whereas the destructive processes were more distinct in the control group [5]. The effectiveness of electrostimulation in the prevention of muscular atrophy in cases of diverse trauma to the skeletomusclar system was also demonstrated in clinical practice [6-8].

In prior studies using electromyostimulation during 30-day AOH, it was possible to maintain orthostatic stability and physical efficiency in man [9-10]. However, the preventive effect of electromyostimulation was appreciably lower than the effectiveness of physical conditioning and combination thereof with lower body negative pressure. Nevertheless, considering the results of other studies [11-16], we can conclude that a course of electrostimulation of muscles may be an effective ancillary method of preventing neuromuscular disorders during space flights.

At the same time, in order to use electrostimulation of muscles as a preventive method during space flights, further investigations must be pursued for the purpose of reducing the number of electrodes applied and simplifying the method of electrostimulation.

BIBLIOGRAPHY

1. Mihaylov, V. M., and Georgiyevskiy, V. S. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1976, pp 37-41.

2. Mogendovich, M. R. "Reflex Interaction Between Locomotor and Visceral Systems," Leningrad, 1957.

3. Idem, "Lectures on Physiology of Visceromotor Regulation," Perm', 1972.

4. Portugalov, I. V.; Il'ina-Kakuyeva, Ye. I.; and Starostin, V. I. KOSMICHESKAYA BIOL., No 1, 1975, pp 9-13.

5. Cherepakhin, M. A.; Kakurin, L. I.; Il'ina-Kakuyeva, Ye. I.; et al. Ibid, No 2, 1977, pp 64-68.

6. Misyuk, N. S. in "Minskiy med. in-t. Kafedra nervnykh bolezney. Klinicheskaya bol'nitsa g. Minska 2-ya. Nauch. konf. nevropatologov 2-ya. Materialy" [Proceedings of Second Scientific Conference of Neuropathologists of the Minsk Medical Institute, Chair of Nervous Diseases and Second Clinical Hospital of Minsk], Minsk, 1965, pp 36-40.

7. Obrosov, A. N., and Liventsev, N. M. "Electrodiagnostics and Electrostimulation of Muscles in the Presence of Peripheral Nerve Lesion," Moscow, 1953.

8. Tariverdiyev, D. D. in "Kaluzhskoye obl. nauch. o-vo travmatologov-ortopedov. Kaluzh. obl. bol'nitsa. Nauch-prakt. konf. Materialy" [Proceedings of Scientific and Practical Conference of the Kalzuhskaya Oblast Scientific Society of Traumatologists and Orthopedists, and Kaluzhnaya Oblast Hospital], Kaluga, 1968, pp 72-75.

9. Georgiyevskiy, V. S.; Gornago, V. A.; Divina, L. Ya.; et al. KOSMICHESKAYA BIOL., No 6, 1973, pp 61-68.

10. Katkovskiy, B. S.; Machinskiy, G. V.; Toman, O. S.; et al. Ibid, No 4, 1974, pp 43-47.

11. Balakhovskiy, I. S.; Bakhteyeva, V. T.; Beleda, R. V.; et al. Ibid, No 4, 1972, pp 68-72.

12. Beregovkin, A. V., and Kalinichesnko, V. V. Ibid, No 1, 1974, pp 72-76.

13. Voskresenskiy, A. D.; Yegorov, B. B.; Pestov, I. D.; et al. Ibid, No 4, 1972, pp 28-32.

14. Drozdova, N. T., and Grishina, Ye. P. Ibid, pp 46-69.

15. Krasnykh, I. G. Ibid, No 1, 1974, pp 68-71.

16. Yakovleva, I. Ya.; Baranova, V. P.; Kornilova, L. N.; et al. Ibid, No 4, 1972, pp 49-54.

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EFFECT OF VESTIBULAR STIMULI ON VISUAL TRACKING IN A LIMITED TRACKING AREA

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No 6, 1979 pp 44-48

[Article by V. I. Babiyak, Yu. N. Kholodov and Yu. K. Yanov, submitted 11 Oct 77]

[English abstract from source]

The paper presents the results of studying visual tracking of the targets which moved with a constant amplitude of angular displacement. The tracking was carried out during an interaction of vestibular and optic sensors. The tracking stability was related to the coincidence of the direction of vestibular and optic stimuli.

[Text] Investigation of the function of the visual analyzer as it applies to objectives of aerospace medicine is one of the pressing problems referable to increasing the reliability of manned aircraft. Some advances have been made in research on motor components of vision [1-5], but the functions of the visual analyzer in the presence of many factors have not been sufficiently studied. We submit here the results of a study of the function of visual tracking of targets, the movement of which was characterized by a constant amplitude of angular displacement. Tracking was performed against the background of interaction between the vestibular and visual analyzers.

Methods

The vestibular and visual analyzers were stimulated separately or together on a special vestibulooptokinetic stand [2] consisting of an optikinetic cylinder (OKC) 2 m in diameter, the axis of rotation of which was superimposed over the angle of rotation of the vestibulometric chair (VMC) situated within the OKC. There was a program device to control rotation of OKC and VMC, which set the magnitude and direction of constant angular acceleration separately for each of the rotating elements. Eye movement was recorded by the method of electrooculography using a direct current amplifier with high resolution. The subject's head was immobilized (in order to prevent involuntary movement) on a special headrest secured to the back of the VMC.

Optokinetic stimuli (OKS) consisted of alternating black and white bands painted vertically on the inner surface of the OKC (Figure 1). The length of the arc of the white band corresponded to an angle of 23.5° and that of the black band to 6.5°. The central angle of the sector formed by two adjacent OKS constituted 30°. OKS were delivered to the constant tracking area contained within the borders of the peep hole ["vision slot"] on a light-proof screen concentrically curved in relation to the cylinder circumference over an arc 1.95 m in diameter. To prevent perception of OKS beyond the area of the peep hole (i.e., to "protect" peripheral vision against OKS), the central angle of the sector formed by the edges of the screen constituted 110°. The slit had a 50 mm opening, its edges and the screen were symmetrical in relation to the subject's eyes. The level of the peep hole was adjusted individually, according to the height of the line of vision. The central angle of the tracking area formed by the peep hole equaled the angle of the sector formed by two adjacent OKS. This made it possible to single out the movement of a single OKS in the opening of the peep hole. There was continuous alternation of OKS in the tracking area during rotation of the VMC or OKC (the time that one stopped moving coincided with the start of movement of the next OKS), reproducing the periodic oscillation of one target. The angular displacement of the target per oscillation changed in accordance with a close to linear law. The amplitude of angular displacement of the target was constant, and it constituted 30°. The period of oscillations depended on the angular rate of rotation of the OKS in relation to the tracking area. Period $T(t)$ of each oscillation was recorded by a photosensitive cell aligned with the edges of the slot. Illumination of the area of the cylinder (OKS) hitting the opening of the slot was provided by the scattered light from an incandescent bulb by means of a specially constructed circular lamp. Illumination of the cylinder constituted 150 lux. Eye movement was recorded simultaneously with period $T(t)$ (Figure 2). In all of the tests, the subject deliberately watched for appearance of the anterior front of the black band through the slot for the purpose of tracking it. Cyclic repetition (without pauses) of this process during the test was indicative of appearance of so-called active optokinetic nystagmus (OKN) during the tracking process. On the tracing, tracking movements of the eyes consist of two components: slow, during tracking time T_C (during this time the visual analyzer receives information about the angular location of the target) and rapid, which is in the opposite direction to encounter the next target. This turn of the eyes was associated with loss of information about angular location of the target, since the eyes do not track the target until it is completely out of the slot range and they do not have time to instantly catch it at the time of appearance, since part of the time is spent on having the eyes "jump" back. Loss of angular location of the target by the tracking system of the eyes was estimated according to mean angular velocity of the target during period $T(t)$:

$$T(t) = \varphi_0\left(1 - \frac{T_c}{T(t)}\right) = \varphi_0 K_n,$$

where ϕ_0 is the central angle of the tracking area (30°) and $K_{\Pi} = 1 - \frac{T_c}{T(t)}$ is the coefficient of angular loss.

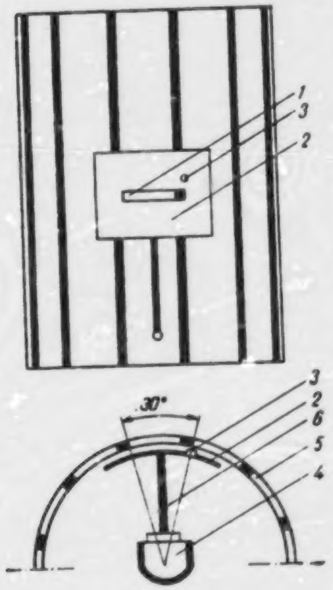

Figure 1.
Arrangement of vestibulo-optokinetic stand
1) tracking area (peep hole)
2) light-proof screen
3) photosensitive cell
4) VMC
5) OKC
6) bracket holding VMC screen

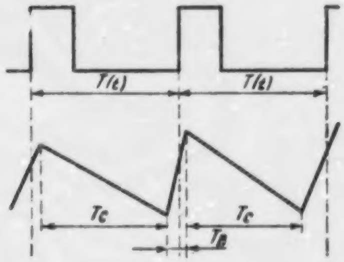

Figure 2.
Tracking time plot; explanation is given in the text

Processing of the obtained data included measurement of $T(t)$ and T_c within the range of measured $T(t)$ according to electrooculogram tracings (see Figure 2).

Conjugate interaction between the vestibular and visual analyzers refers to coinciding direction of the slow component of vestibular nystagmus and tracking eye movement [2, 4]. Coincidence of the tracking phase with the rapid component of nystagmus is interpreted as an antagonistic combination of interaction. There are also certain differences in manifestations of rotatory and postrotatory nystagmus. For this reason, four rotations with stimulation of the vestibular system are needed to examine antagonistic and and conjugate interaction of the two analyzers (with due consideration of direction of tracking and sign of angular acceleration). In addition, two OKC rotations without vestibular stimulation are required. Thus, the complete study program includes six rotations (Figure 3). All are performed following a trapezoid program, with a constant angular acceleration of 5.4°/s^2.

In the first series of studies (see Figure 3, I) we expected to obtain information about the pass band of the oculomotor system for angular OKS velocity. Its transmission capacity was evaluated on the basis of disruption of tracking (during build-up of OKS velocity) and restoration thereof (when OKS movement slowed down).

In the second series of studies (see Figure 3, II), the VMC was rotated at an acceleration of 5.4°/s^2, and OKC was rotated in the same direction at an advancing acceleration of $10.8°/s^2$. This made it possible to guide the OKS in the direction of VMC rotation, in relation to the subject, at an acceleration of $5.4°/s^2$ and to use the antagonistic combination of tracking and rotatory nystagmus. The VMK and OKC rotation was slowed down at the same acceleration levels, and conjugate tracking with postrotatory nystagmus occurred at this time.

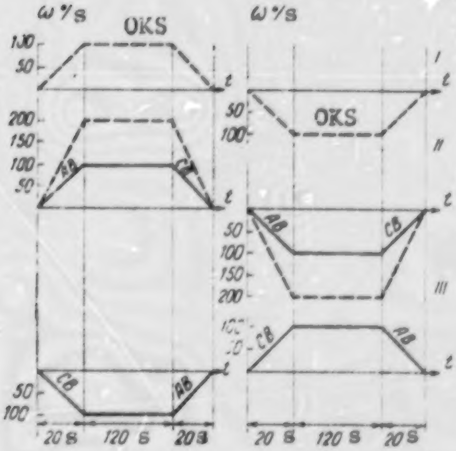

Figure 3.
Program of tests.
Here and in Figure 4:
AB) antagonistic interaction
CB) conjugate interaction.
Explanation is given in the text.

In the third series of studies we only rotated the subject at an acceleration of $\pm 5.4°/s^2$ (Figure 3, III). In this case, the relative movement of OKS was directed opposite to the direction of rotation of the subject, and this provided for a conjugate combination of tracking and rotatory nystagmust, antagonistic and postrotatory nystagmus. These studies were conducted on 11 men ranging in age from 20 to 22 years, with normal peripheral and central vision, and good resistance to vestibular motion sickness (the subjects were specially screened on the basis of endurance of 10-min exposure to Coriolis accelerations).

Results and Discussion

Figure 4 illustrates the curves of changes K_{Π} as a function of angular velocity of OKS in the three series of studies (see Figure 3) on one of the subjects.

The following patterns were demonstrated in optikinetic tracking in the absence of vestibular stimuli: even tracking of OKS within the tracking area is performed up to an angular velocity of 25-36°/s; synchronization of tracking eye movements from the time of appearance of the next target (OKS), already associated with saccadic movements (along the tracking route) occurs in different subjects at angular velocities of 25-36 to 40-54°/s; the top range of angular velocity of OKS at which the target is still tracked is 2.5-3% higher for eye movements from left to right than from right to left; the maximum angular rate of tracking movements of the eyes in the region of disruption (with increasing velocity of OKS) and restoration of tracking (with decreasing velocity of OKS) is not the same: restoration of tracking occurs at higher values of angular rate of eye movements (by-6-9%); with increase in angular velocity of OKS there is an increase in angular speed of "jump" back to the next target, which leads to relatively reduction of K_{Π}. When the angular velocity of OKS diminishes, conditions are created where tracking is faster than movement of the target, and this leads to relative increase of K_{Π}.

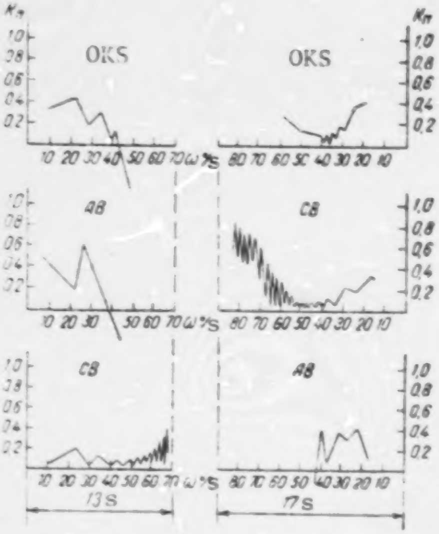

Figure 4.
Results of tests following program graphically illustrated in Figure 3 during unidirectional rotation of a subject

Experiments dealing with interaction of vestibular and visual analyzers are indicative of latent reserves for rapid action by the oculomotor system, the possibility of expression of which depends on the nature of interaction between these analyzers: conjugate interaction, which occurs when there is coincidence of slow components of optokinetic and vestibular nystagmus, improves tracking quality; antagonistic, when these components are opposed to one another, worsens the quality of tracking. In the case of antagonistic effect of vestibular stimulation on optokinetic function of the visual analyzer, only brief tracking is possible, due to the drastic reduction of the tracking phase. In this case, tracking time is commensurate with the "jump" back, and tracking is characterized by instability, which is manifested by fluctuation of K_{Π} (increasing amplitude of oscillation; see Figu Figure 4). In the case of antagonistic interaction between the vestibular and visual analyzers, there is significant increase in dissimilarity of tracking speed in the region of disruption and restoration thereof, as compared to the base level, and postrotatory nystagmus has a more marked influence on tracking parameters, other conditions being equal.

As shown by the results of this study, a certain reserve of rapid action is inherent in oculomotor function that implements tracking of a recurrent [cyclic] target that moves in one direction (serrate oscillation). However, there is a limit to this reserve (considering that peripheral parts of the retina are excluded from the tracking process) when the angular velocity of OKS is of the order of 36°/s. Higher angular rates of rotation of the eyeball over the entire route of angular displacement of the target are related to intensive contraction of ocular muscles. In the case of cyclic function, such a tracking mode is apparently disadvantageous from the standpoint of energy, since it leads to fatigue of the oculomotor system and increased relaxation ["inertia"] thereof. Adjustment of angular rate by concurrent decrease in amplitude of eye movements diminishes the energy expended on tracking; however, such adjustment is related to loss of tracking stability, leading to disruption thereof. Intervention of the vestibular system in the case of a conjugate combination of interaction leads to improvement of quality of regulation, for which reason it becomes possible to use its reserve stability. The antagonistic combination of analyzer interaction increases inertia of the tracking system of the eyes, and this is particularly manifest during the period when the eyes "jump" back. The latter circumstance leads, already at the start of tracking, to loss of stability, related to the natural loss of phase advance due to increase in duration of the return saccadic movement. For this reason, restoration of stable tracking over period $T(t)$ along angular displacement also becomes impossible, due to loss of some of the time on the jump itself. The dynamics of K_{Π} oscillations (see Figure 4) during the tracking phases reflect the nature of stability (instability) of regulation, which depends on the intervention of the vestibular analyzer.

These results can be used to define the parameters of the functional norm for the tracking system of the eyes in the presence of vestibular stimuli.

BIBLIOGRAPHY

1. Andreyeva, Ye. A.; Vergiles, N. Yu.; and Lomov, B. F. in "Motornyye komponenty zreniya" [Motor Components of Vision], Moscow, 1975, pp 7-55.

2. Kurashvili, A. Ye., and Babiyak, V. I. "Physiological Functions of the Vestibular System," Leningrad, 1975.

3. Idem, "Electronystagmography," Leningrad, 1970.

4. Leushina, L. I. in "Fiziologiya sensornykh sistem" [Physiology of Sensory Systems], Leningrad, Pt 1, 1971, pp 60-87.

5. Yarbus, A. L. "The Role of Eye Movements in the Vision Process," Mosocw, 1965.

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ROLE OF INTEROCEPTIVE AFFERENTATION IN FUNCTION OF THE CORTEX OF THE VISUAL ANALYZER

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 48-53

[Article by N. I. Pityk, submitted 7 May 77]

[English abstract from source]

The experiments on diplacin-immobilized rats showed that stimulation of gastric and rectal mechanoreceptors caused noticeable changes in the control and light-induced impulse activity of neurons of the optic cortex (field 17). The predominant pattern of cell reactions were tonic changes of impulsation. They included both stimulatory and inhibitory effects. The latter occurred mostly as a result of stimulation of gastric mechanoreceptors. Changes in the evoked activity of those neurons involved most frequently enhancement or inhibition of responses, contrasting and stabilization of short-latent responses, and their masking with neuronal noise. The paper discusses the functional importance of the above changes in the control and evoked activities of neurons of the optic cortex during interoceptive effects as well as possible central pathways of their realization in the optic cortex.

[Text] At the present time, it is known that flights under both hypergravity and weightless conditions are often associated with onset of various sensory disorders in pilots, including changes in functions of the visual analyzer, which is the main channel of access of information to the brain concerning the existing flight situation. There is impairment of functional organization of analyzers involved in analysis of spatial relations, and this is reflected in the level of overall stability of the nervous system in the presence of flight factors, leading to a change in operational efficiency, decrease thereof in most cases [1-7].

Some authors relate disturbances of visual perception to appearance during flight of unusual afferent influnces from various mechanoreceptors, including interoceptors of internal organs and cerebral parts of the analyzer [3, 5-7, 8]. However, there have been virtually no experimental studies of this problem.

For this reason, our objective here was to investigate interoceptive influences on neuronal impulsation in field 17 of the cerebral cortex.

Methods

Tests were conducted on 17 adult waking cats immobilized with diplacin, conducting acute experiments. The animals were surgically prepared for the experiments under local anesthesia. We used glass microelectrodes filled with 3 M KCl solution, with resistance of 8-28 $M\Omega$, to record impulse activity of single neurons of the visual cortex. After input in the cathode follower of an alternating current amplifier, the potentials were recorded on film [cinematographic] from the screen of a cathode oscillograph, as well as magnetic tape. We used a 4-channel neurograph in the experiments.

Stimulation of mechanoreceptors of the stomach and rectum, induced by distention of their walls by insufflating a balloon of thin rubber inserted in the organ (pressure of 20-60 mm Hg) served as a model of interoceptive stimulation. In some experiments, we also stimulated the reticular formation of the mesencephalon (F +4) through bipolar nichrome electrodes introduced stereotactically [9]. We used series of square-wave pulses at a recurrence frequency of 100-200 Hz in a series. The retina of the atropinized contralateral eye was submitted to photostimulation with single flashes of light lasting 10-50 ms at a recurrence frequency of 0.1-0.3 Hz.

Analysis was made of impulsation activity of neurons by means of charts of current mean frequency and poststimulation histograms [10]. We recorded the effect of interoceptive stimulation only in those cases where the changes in integral mean frequency of neuronal activity constituted at least 25% of the base values.

The reliability of obtained data was determined using biometric methods [11]. In all, we tested 122 neurons of filed 17 of the cerebral cortex.

Results and Discussion

Stimulation of mechanoreceptors of the stomach and rectum induced statistically reliable changes in background impulse activity in a mean of 44% of the tested neurons in cortical field 17 (see Table). Both inhibitory and enhancing effects were observed. Prolonged tonic changes in impulse activity were the prevalent form of cell reaction to interoceptive stimulation (Figure 1). In response to stimulation of gastric mechanoreceptors, tonic reactions were observed in 95% of the responding neurons and reactions to distention of the intestine were observed in 85.3%. Complex reactions appeared in a few neurons (8 units), manifested by initial activation of cells followed by depression of impulse activity, or vice versa.

Variance analysis revealed that the tested interceptive stimuli had a significant, statistically reliable effect on impulse activity of neurons of the visual cortex (see Table). For example, the influence of gastric mechanoreceptors on development of inhibition of neuronal activity constituted 14 to 36% of the force of all factors determining the magnitude of changes in impulse activity of neurons in this direction. We had observed similar changes in background neuronal activity upon interoceptive stimulation previously on the level of the external geniculate bodies [12, 13], and other authors observed them in the neuronal system of the vestibular nuclei [14].

Effect of stimulation of mechanoreceptors of the stomach and intestine on background activity of neurons of the visual cortex

Statistical index of changes in neuronal activity	Stomach		Intestine	
	inhibitory influence (n=16)	excitatory influence (n=11)	inhibitory influence (n=17)	excitatory influence (n=18)
$d \pm m$	−67,3±21,4%	+282,2±105,6%	−65,3±20,8%	+133,9±40,1%
t	3,138	2,672	3,142	2,485
P	<0,01	<0,02	<0,01	<0,01
$\eta_x^2 \pm m$	0,253±0,026	0,206±0,031	0,207±0,025	0,185±0,026
$\bar{\eta}_x^2$	0,14—0,36	0,08—0,34	0,11—0,31	0,05—0,27
F	9,48	6,33	8,35	6,01
β	>0.99	<0,95	>0,99	>0,95

Key: $d \pm m$) difference between overall mean frequencies (%)
t) criterion of Student
$\eta_x \pm m$) general index of force of influence
η_x^2)confidence range of force of tested factor
F) criterion of Fisher
β) threshold of probability of error-free forecasts

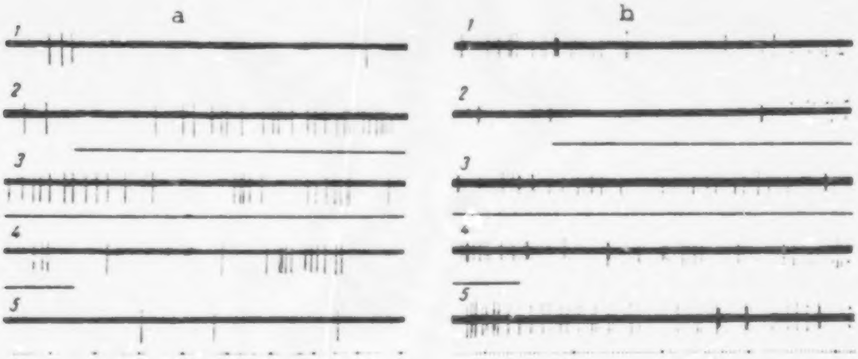

Figure 1. Activation (a) and depression (b) of neuronal activity in the cat's visual cortex during stimulation of rectal mechanoreceptors. Straight line is mark of distention period. Time mark, 1 s

1) background
2,3) neuronal reaction to distention of organ walls
4,5) reaction to collapse of walls

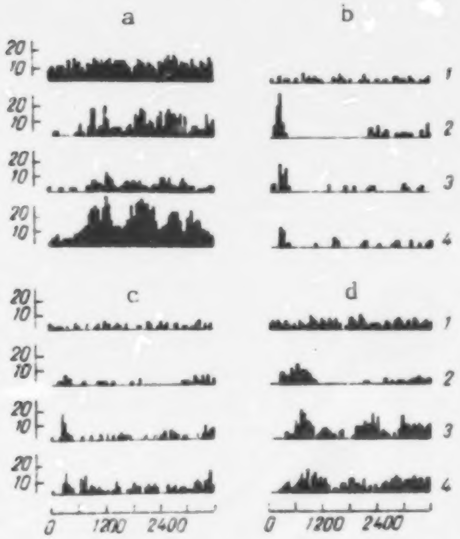

Figure 2.

Types of changes in responses of visual cortex neurons to flash of light during stimulation of internal organs.

X-axis, time (ms); y-axis, mean number of impulses per 60 ms. Time of the flash corresponds to start of histograms

a) changes in long latent component of responses
b) depression of short latent response
c) stabilization of response
d) "masking" of sensory response
1) background
2) background response to flash
3,4) neuronal response to flash against background of stimulation of mechanoreceptors of stomach and rectum, respectively

At the same time, some differences are demonstrable in the direction of changes in spike activity of visual neurons upon stimulation of gastric and intestinal mechanoreceptors. While distention of the stomach more often induced neuronal reactions in the form of prolonged (for tens of seconds) decrease in amplitude of impulsation (a mean of 60% of the units, in relation to those that reacted to this type of interoceptive stimulation) (see Figure 1), upon stimulation of rectal mechanoreceptors elicited both excitatory and inhibitory changes in impulse activity. These differences in neuron reactions to stimulation of gastric and rectal mechanoreceptors could be attributable both to the dissimilar quantitative and qualitative composition of visceral afferent elements carrying impulses from these organs to the brain, and apparently to the distinctions of organization of their ascending projections and inclusion of afferent signals they transmitted in central mechanisms of integration. The above-described changes in background activity of neurons of the visual cortex upon stimulation of gastric and intestinal mechanoreceptors are quite similar in their characteristics to the reactions of these neurons to electrostimulation of the vagi and splanchnic nerves [15], between the projections of which it is believed there are basic differences [16]. Prevalence of inhibitory neuronal reactions to stimulation of the vagi was also noted in the vestibular nuclei [17, 18].

Some of the responding neurons reacted by a decrease or increase in frequency of generated impulses throughout the period (60 s) of interoceptive stimulation. In some cells, inhibition lasted for a shorter time and the frequency of impulsation gradually reverted to the base level, in spite of continuing interoceptive stimulation. Most of these cells reacted not only to distention of the gastric or intestinal walls, but collapse thereof as well (see Figure 1).

Interoceptive stimuli also led to substantial and rather diverse changes in neuronal activity in field 17 of the visual cortex induced by flashes of light (in an average of 38% of the tested cells). Most often these changes were manifested by intensification or depression of the long-latent components of the responses (Figure 2a), filling of inhibitory pauses, extension or shortening of the latter. In some neurons there was contrasting of responses to the flash during interoceptive stimulation, with isolation thereof from the background due both to inhibition of the latter and enhancement of the response itself (Figure 3b). We observed an analogous direction of changes in photic responses of these neurons upon stimulation of the reticular formation of the midbrain (Figure 3c). These influences can last for several seconds after discontinuing reticular stimulation. Distinct and stable discharges (Figure 2c) appeared in response to the flash against the background of interoceptive stimulation in three neurons that had responded to light irregularly. Such types of functional interaction between interoceptive and visual stimuli were demonstrated by us on the level of the external geniculate bodies [13, 19]. For this reason, it can be assumed that the phenomenon of contrasting and stabilization of sensory-specific visual responses of neurons, observed on both the cortical and thalamic levels of the visual sensory system with a change in interoceptive afferent influx to the brain, could be one of the elements in the mechanism of enhancement of resolution capacity of the visual analyzer, which has occasionally been observed during space flights [1, 7, 20, 21].

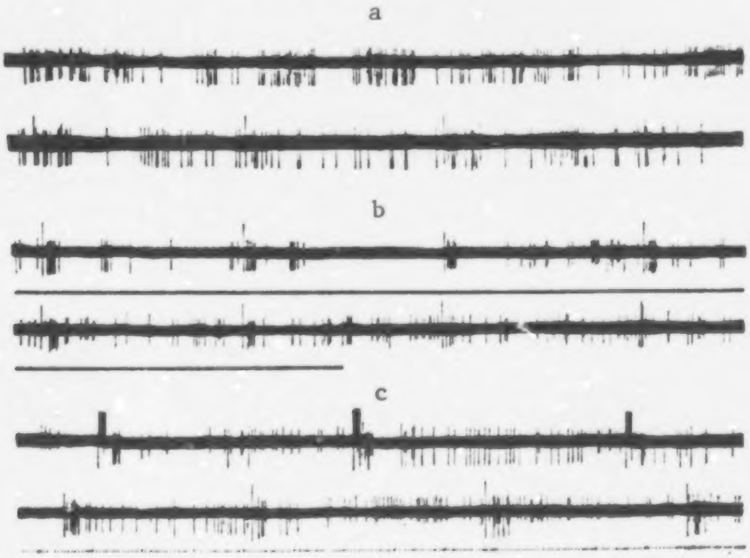

Figure 3. Contrasting of visual cortex neuronal response to light with interoceptive (b) and reticular (c) stimulation (a--background and background reactions to light). The line marks interoceptive stimulation; single artifacts refer to flashes, series of artifacts refer to time of stimulation of the mesencephalic reticular formation. Time mark, 1 s.

In some cases, an increase in frequency of neuronal discharges during interoceptive stimulation caused "masking" of neuronal reactions to light (Figure 2d). In other words, neuronal impulsation induced by stimulation of interoceptors emerges as "neuronal noise" obscuring the sensory-specific responses of visual cortical cells. There may be impairment of dynamics of cortical mechanisms of processing visual information coming to the brain and adequate evaluation of its parameters, which in turn could be one of the causes of impaired visual perception of the surroundings, in particular, decreased visual contrast sensibility, deterioration of operational visual efficiency, which are not uncommonly observed during flights [1, 2, 22].

The analogous nature of interoceptive and reticular effects on photic responses of some of the tested neurons warrants the belief that activation of ascending systems of the reticular formation of the mesencephalon is one of the central mechanisms of involvement of neurons of the visual cortex in the reaction during interoceptive stimulation and appearance of diverse forms of functional interaction between the latter and sensory-specific signals. There may be other pathways for expression of interoceptive influences on the neurons of the visual cortex. We refer, first of all, to the structures of the limbic system and hypothalamus, which represent the most important level of integration of visceral functions [23]. This hypothesis is backed up by data in the literature, according to which, direct projections of visceral systems are demonstrable in the limbic system and hypothalamus [24, 25], in the first place; in the second place, the hypothalamus has direct afferent ties with the visual cortex and external geniculate bodies [26] and, in the third place, various parts of this structure have a modulating influence on the activity of neurons of the visual cortex [27-29]. All this enables us to interpret the neuronal reactions in the visual cortex, which are observed with interoceptive influences, not only as the result of general nonspecific activation of cortical neuronal systems, but the consequence of specific and selective influences on the function of cortical regions involved in formation of sensations.

Thus, interoceptive afferent signals have a substantial influence on the level of "adjustment" ["tuning"] and functioning of the cortical part of the visual analyzer. The obtained data indicate that unusual afferent influences, in particular from interoceptors of the viscera, play an important role in mechanisms of development of sensory (including visual) disorders during flights involving weightlessness and hypergravity.

BIBLIOGRAPHY

1. Ivanov, Ye. A.; Popov, V. A.; and Khachatur'yants, L. S. in "Nevesomost'" [Weightlessness], Moscow, 1974, pp 341-380.

2. Kitayev-Smyk, L. A. Ibid, pp 41-66.

3. Kovalenko, Ye. A. Ibid, pp 237-278.

4. Baranovskiy, V. V.; Yemel'yanov, M. D.; and Kuznetsov, A. G. ZH. VYSSH. NERVN. DEYAT. [Journal of Higher Nervous Activity], No 6, 1962, pp 1001-1010.

5. Komendantov, G. A., and Kopanev, V. I. in "Nevesomost'," Moscow, 1974, pp 75-83.

6. Savin, B. M. "Hypergravity and Functions of the Central Nervous System," Leningrad, 1970.

7. Yuganov, Ye. M., and Kopanev, V. I. in "Osnovy kosmicheskoy biologii i meditsiny" [Fundamentals of Space Biology and Medicine], Moscow, Vol 2, Bk 2, 1975, pp 173-197.

8. Brown, J. Z. AEROSPACE MED., Vol 32, 1961, pp 209-217.

9. Reinoso-Suarez, F. "Topographic Atlas of the Cat Brain for Experimental Physiological Research," Darmstadt, 1961.

10. Meshcherskiy, R. M. "Analysis of Neuronal Activity," Moscow, 1972.

11. Plokhinskiy, N. A. "Biometry," Moscow, 2d edition, 1970.

12. Pityk, N. I. NEUROFIZIOLOGIYA [Neurophysiology], No 3, 1973, pp 246-253.

13. Pityk, N. I.; Raytses, V. S.; and Khananashvili, M. M. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 4, 1975, pp 537-544.

14. Dutov, A. M. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 8, 1974, pp 10-13.

15. Pityk, N. I. NEUROFIZIOLOGIYA, No 4, 1977, pp 361-367.

16. Kostyuk, P. G., and Preobrazhenskiy, N. N. "Mechanisms of Integration of Visceral and Somatic Afferent Signals," Leningrad, 1975.

17. Ayzikov, G. S.; Malikova, S. N.; and Radkevich, L. A. NEYROFIZIOLOGIYA, No 5, 1976, pp 507-513.

18. Raytses, V. S., and Shlyakhovenko, A. A. FIZIOL. ZH. SSSR, No 3, 1972, pp 377-384.

19. Pityk, N. I. NEYROFIZIOLOGIYA, No 6, 1973, pp 636-643.

20. Berry, Ch. AEROSPACE MED., Vol 41, 1970, pp 500-519.

21. O'Lone, R. G. AVIAT. WEEK AND SPACE TECHNOL., Vol 83, No 9, 1965, pp 51-53.

22. Barer, A. S. KOSMICHESKAYA BIOL. [Space Biology], No 1, 1967, pp 57-64.

23. Newman [N'yumen], P. in "Current Trends in Neurophysiology," Leningrad, 1977, pp 201-216.

24. Baklavadzhyan, O. G.; Adamyan, F. A.; and Avetisyan, E. A. NEYROFIZIOLOGIYA, No 3, 1973, pp 253-260.

25. Zambrzhitskiy, I. A. "The Limbic Region of the Cerebrum," Moscow, 1972.

26. Sacai, K.; Leger, L.; Salvert, D.; et al. EXPERIENTIA, Vol 31, 1975, pp 1350-1352.

27. Kozhechkin, S. N.; Zhadina, S. D.; Bondar', G. G.; et al. ZH. VYSSH. NERVN. DEYAT., No 6, 1975, pp 1274-1283.

28. Latash, L. P., and Kuman, E. A. NEYROFIZIOLOGIYA, No 4, 1971, pp 359-367.

29. Raytses, V. S.; Pityk, N. I.; Shlyakhovenko, A. A.; et al. in "Vsesoyuznaya konf. po fiziologii vegetativnoy nervnoy sistemy. 4-ya. Materialv" [Proceedings of 4th All-Union Conference on Physiology of the Autonomic Nervous System], Yerevan, 1976, p 253.

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EFFECT OF ACUTE HYPOXIA ON SPECIFIC AND NONSPECIFIC SYSTEMS OF THE RABBIT BRAIN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 6, 1979 pp 53-57

[Article by N. S. Akopyan and O. G. Baklavadzhyan, submitted 17 Aug 77]

[English abstract from source]

At a simulated altitude of 8500-9000 m, an increase in the amplitude of the early positive and negative phase of the thalamic-cortical evoked potentials, and a slight prolongation of the latent period were seen. Changes in the reticulo-cortical and hypothalamo-cortical evoked potentials included a pronounced inhibition of their negative phase. In the EEG slow delta-waves increased gradually, becoming the major rhythm. The presence of EEG signs of the development of inhibitory processes in the cortex suggested that the changes in evoked potentials were also a result of inhibition of cortical neurons. Hypoxia-adapted rabbits tolerated acute hypoxia much better. They exhibited less pronounced changes in the electric manifestations of the function of specific and nonspecific projection systems of the brain.

[Text] Electrical activity of the brain under hypoxic activity is studied mainly with the use of the EEG. Evoked potentials (EP) were recorded primarily when studying hypoxia produced by means of bloodletting [1-3]. In this work, we investigated the influence of acute hypoxia on thalamocortical (TCEP), hypothalamocortical (HCEP) and reticulocortical (RCEP) evoked potentials in chronic experiments on rabbits "lifted" in a pressure chamber and acclimated to high altitudes.

Methods

This study was pursued on 24 rabbits, in whom active bipolar electrodes were placed in the posterior ventral nucleus [specific] of the thalamus, reticular nucleus of the tegmentum of the mesencephalic reticular formation and posterior nucleus of the hypothalamus. Monopolar silver electrodes were implanted in the occipital, sensomotor and temporal regions of the cerebral cortex. The silent electrode was fixed in the bones of the frontal sinus. We recorded the TCEP (specific), RCEP and HCEP (nonspecific), as well as EEG, respiration and EKG Mild (threshold) and strong (supraliminal) stimuli were used to produce 's. The force of stimulation that elicited a series of similar low-amplitude EP's was taken as the threshold. EP's of maximum amplitude were obtained with supraliminal force of stimuli. The parameters were recorded prior to exposure to high altitude, immediately after the "climb" in the pressure chamber to an "altitude" of 8500-9000 m and after "descending" to atmospheric pressure. EP's were recorded on a CI-18 oscillograph and duoscope, while the EEG, respiration and EKG were recorded on a 17-channel electroencepahlograph. An ES-4M stimulator with radiofrequency output was used to deliver electric stimuli to subcortical nuclei. We delivered single square-wave pulses lasting 0.1-0.2 ms, with threshold voltage of 2-5V and supraliminal voltage of 3-10 V. We determined the accuracy of placement of the tips of the implanted electrodes on sections prepared with a freezing microtome. In a second series of experiments, 14 rabbits were taken up to a high-altitude region (Nor-Ambert, Aragats) at 2200 m after obtaining background data. We repeated the tests in the pressure chamber after 4 months of acclimatization.

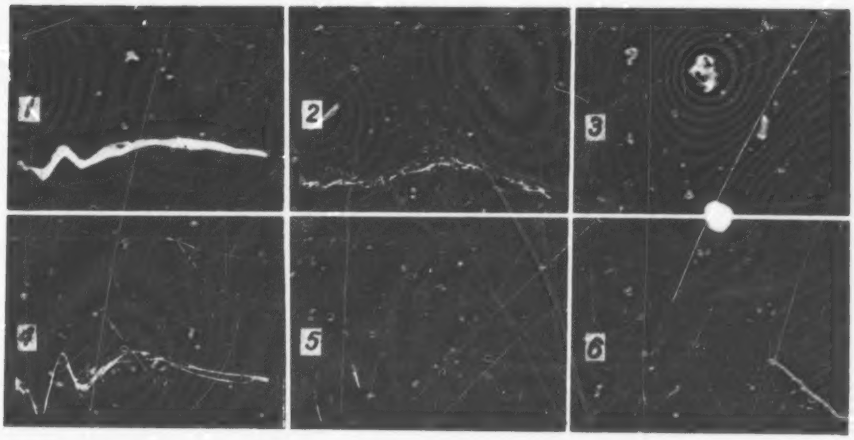

Figure 1. Changes in TCEP of nonacclimatized animal with hypoxia.

Here and in Figure 2:

1-3) before "climb," at 8500 m and after "descent" with threshold stimulation, respectively

4-6) the same with supraliminal stimulation.

Calibration 10 ms, 20 µV.

Results and Discussion

As a result of studies of specific TCEP, it was established that multicomponent EP are recorded from the sensorimotor region of the cortex prior to ascent in the pressure chamber (Figure 1); they are notable for a relatively short latency period (2.35±0.2 ms) and high amplitude of initial positive and negative components with supraliminal stimulation (350±32.5 and 305±24.6 μV). Biphasic and multiphasic RCEP and HCEP are recorded in the visual and sensorimotor regions of the cerebral cortex, with latency periods of 3.77±0.2 and 3.65±0.21 ms, respectively. The amplitude of the initial positive RCEP wave was 307±25 and that of the negative wave was 227±21 μV, while for HCEP the figures were 316±35 and 270±21 μV, respectively.

After ascending to an "altitude" of 8500-9000 m, there was no evoked response to mild stimulation of the specific thalamic nucleus, where stable two-component EP's were recorded prior to the "climb." In response to strong stimulation there was an increase to 415±34 μV in the positive phase of TCEP and to 323±39 μV in the negative one, as well as extension of the latency period to 2.83±0.2 ms. After "descent" to atmospheric pressure, we observed a gradual restoration of initial values for these parameters (see Figure 1).

In the presence of acute hypoxia there were distinctive changes in RCEP and HCEP. In both cases, there was drastic depression of the negative wave of EP. The negative phase of RCEP decreased to 32±7 μV and that of HCEP to 45±12 μV, or by 90-95% of the base level. In some animals, the negative phase disappeared at an "altitude" of 8500-9000 m, and instead of a polyphasic or biphasic EP there were single-phase positive potentials. At the same time there was some extension of the latency period. With a threshold stimulus delivered to subcortical nuclei, there was no evoked response at a high "altitude," whereas distinct EP's were obtained prior to the "ascent."

In several experiments, the rabbits were lifted to "altitudes" of 10,000-11,000 m. In this case, the nonspecific EP following strong stimulation did not have a negative wave. The positive phase of EP was more resistant to hypoxia, although the amplitude of the positive wave diminished.

EP changes occurred against the background of intensification of slow delta rhythm on the EEG which, as we know, is an indicator of inhibitory processes in the brain. At high "altitudes," respiration and heart rate diminished markedly, there was general decline of muscle tone, and the animals assumed a lateral position with the head tilted back. Comparable changes in the EEG, EP, respiration, heart function and behavioral reactions in the presence of altitude hypoxia were described in other works [4-11].

In acclimatized rabbits, in response to mild stimulation at the maximum "altitude," we demonstrated low-amplitude potentials which were almost the same as under background conditions. In response to strong stimulation, there were EP's with slightly increased amplitudes of both phases of the initial positive-negative complex of TCEP (Figure 2). In the case of mild stimuli, RCEP and HCEP were characterized only by significant depression of the negative wave under acute hypoxic conditions. With strong stimuli at an "altitude" of 8500-9000 m, the negative phase of these EP's did not undergo such significant deformation. There was only some decrease in amplitude thereof (from 255±20 to 205±14 μV for HCEP, from 263±18 to 238±23 μV for RCEP).

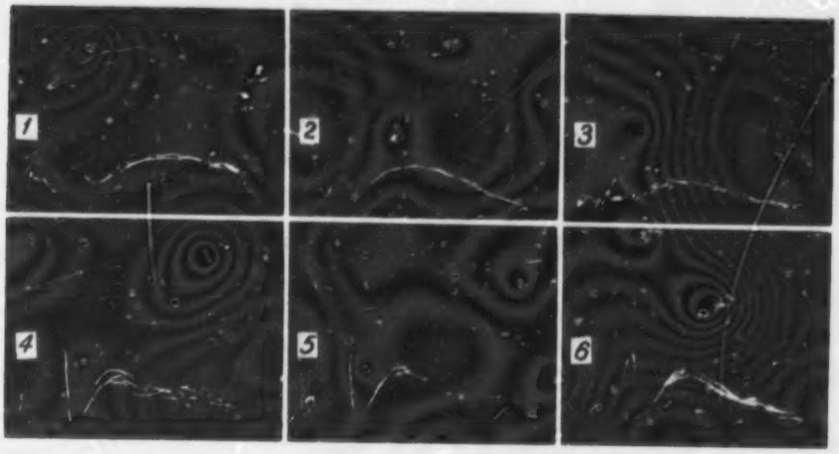

Figure 2. Changes in TCEP of acclimatized hypoxic animal

On the basis of current conceptions of the genesis of EP's [12, 13], the increase in amplitude of both phases of TCEP in the presence of acute hypoxia may be indicative of functional changes in cellular elements of all layers of the cortex. Since the EEG changes at high altitude are indicative of prevalence of inhibitory processes, it may be assumed that the increase in amplitude of TCEP is also the result of inhibition of cortical neurons. This hypothesis appears paradoxical only at first glance. The decrease in ascending nonspecific impulsation due to depression of functions of the activating system of the brain could lead to some hyperpolarization of cortical neuronal membranes. In the case of hyperpolarization of membranes, the amplitude of depolarization postsynaptic potentials, i.e., EP amplitude, increases [14]. Thus, the increase in EP amplitude against the background of slow EEG waves may be considered the result of increased amplitude of axosomatic and axodendritic excitatory postsynaptic potentials, against the background of neuronal hyperpolarization. The increase in amplitude of TCEP suggests that the neurons of the specific thalamic nucleus are more resistant to hypoxia than cortical neurons. With decrease in intensity of the ascending specific discharge due to deterioration of functional state of specific thalamic neurons, apparently we cannot observe an increase in EP amplitude, even against the background of hyperpolarization of cortical neurons. An analogous increase in both components of the primary response may occur during deep sleep under anesthesia [12].

The selective depression of negative wave of RCEP and HCEP of the sensorimotor cortex at the maximum "altitude" merits special attention. The statistically reliable decrease in amplitude of the negative phase of the positive-negative complex of nonspecific EP's and total disappearance thereof with a threshold force of stimulation is most probably related to functional depression of both "nonspecific" axodendritic synapses of the pleximorphic [plexiform?] layer of the cortex and neurons of nonspecific subcortical structures, reticular formation and hypothalamus. With attenuation of ascending activating impulsation from the reticular formation and hypothalamus, there is synchronization of EEG rhythm and decrease in intensity of the nonspecific ascending discharge evoked by delivery of a single stimulus to the mesencephalic reticular formation or hypothalamus. This deficiency of afferentation is demonstrable the most distinctly in the cortical structures that are more sensitive to hypoxia, particularly in apical dendrites of the first, molecular layer of the cortex. The decreased intensity of nonspecific impulsation on the level of axosomatic synapses, which generate the superficial positive phase of EP's, does not appreciably affect the amplitude of this wave, and this is apparently related to the greater resistance to hypoxia of axosomatic synapses of the 3d-4th cortical layers. At first glance, this interpretation of the data is in some contradiction to the conclusions of a number of authors concerning the greater sensitivity of neuronal soma to hypoxia [15, 16]. However, it must be indicated that these authors had in mind only individual structural elements of the neuron itself, rather than the axosomatic and axodendritic synaptic system.

The selective depression of the negative wave of nonspecific RCEP and HCEP may also be related to generalized conduction of a relatively weak flow of impulses over all cortical layers, which is inherent in the nonspecific projection system [13, 17]. While there is generation of the negative wave under normoxic conditions, in the case of hypoxia and deterioration of functional state of the top cortical layers such a flow of impulses is inadequate for generation of this wave. The tendency toward extension of latency period of EP's should also apparently be attributed to "defacilitation" hyperpolarization of cortical neurons as a result of diminished intensity of nonspecific afferent impulsation. The intensification of "recruiting" [?] responses evoked by low-frequency stimulation of nonspecific thalamic nuclei under hypoxic conditions is also indicative of diminished ascending activating impulsation in the presence of profound hypoxia [18]. As we know, there are reciprocal relations between subcortical systems [19, 20]. Evidently the acclimatization effect is related to some reorganization of the body's compensatory reactions, which improve delivery of blood to the brain in the presence of altitude hypoxia.

On the whole, the obtained data indicate that the changes in amplitude and time parameters of EP's depend on a number of factors related to structural organization of the systems studied and sensitivity thereof to hypoxia.

BIBLIOGRAPHY

1. Yanvareva, I. N. in "Mekhanizmy vyzvannykh potentsialov mozga" [Mechanisms of Evoked Potentials of the Brain], Leningrad, 1968, pp 56-58.

2. Idem, Ibid, Leningrad, 1971, pp 48-55.

3. Yanvateva, I. N.; Kuz'mina, T. R.; and Sinyaya, I. S. in "Vsesoyuznaya konf. po elektrofiziologii tsentral'noy nervnoy systemy. 6-ya. Materialy" [Proceedings of 6th All-Union Conference on Electrophysiology of the Central Nervous System], Leningrad, 1971, pp 308-309.

4. Agadzhanyan, N. A.; Dvorzhak, I.; Kalyuzhnyy, L. V.; et al. ZH. VYSSH. NERVN. DEYAT. [Journal of Higher Nervous Activity], No 1, 1971, pp 176-183.

5. Idem, KOSMICHESKAYA BIOL. [Space Biology], No 4, 1970, pp 81-86.

6. Goroyan, G. P., and Kalyuzhnyy, L. V. Ibid, No 5, 1969, pp 28-32.

7. Kalyuzhnyy, L. V.; Agadzhanyan, N. A.; and Zakharova, I. N. Ibid, No 5, 1967, pp 38-45.

8. Malkin, V. B. in "Aviatsionnaya i kosmicheskaya meditsina" [Aviation and Space Medicine], Moscow, 1963, pp 348-352.

9. Kovalenko, Ye. A., and Chernyakov, I. N. "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 21, 1972, pp 21-24.

10. Akopyan, N. S., and Baklavadzhyan, O. G. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 9, 1975, pp 1303-1309.

11. Bashkirov, A. A.; Kichigin, A. V.; Korobkov, A. V.; et al. in "Vsesoyuznaya konf. po elektrofiziologii tsentral'noy nervnoy systemy. 7-ya. Materialy" [Proceedings of 7th All-Union Conference on Electrophysiology of the Central Nervous System], Kaunas, 1976, p 32.

12. Roytbak, A. I. "Bioelectric Phenomena in the Cerebral Cortex," Tbilisi, Pt 1, 1955.

13. Gusel'nikov, V. I. "Electrophysiology of the Brain," Moscow, 1976.

14. Eccles, J. "Physiology of Synapses," Moscow, 1966.

15. Lorente de No, R. J. CELL. COMP. PHYSIOL., Vol 29, 1947, pp 207-213.

16. Gelfan, S., and Tarlov, T. J. NEUROPHYSIOL., Vol 18, 1955, pp 70-77.

17. Beritashvili, I. S. "Structure and Functions of the Cerebrum," Moscow, 1969.

18. Akopyan, N. S., and Baklavadzhyan, O. G. ZH. VYSSH. NERVN. DEYAT., No 5, 1977, pp 1061-1067.

19. Tokisanne, T.; Kowakami, M.; and Gellhorn, E. ARCH. INT. PHARMACODYN., Vol 113, 1957, pp 217-229.

20. Baklavadzhyan, O. G. "Vegetative Regulation of Electrical Activity of the Brain," Leningrad, 1967.

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STUDY OF BIOELECTRIC ACTIVITY OF NEUROMUSCULAR AND SYMPATHETIC SYSTEMS DURING EXPOSURE TO A STEADY MAGNETIC FIELD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 58-61

[Article by L. D. Klimovskaya and S. B. Krotova, submitted 16 Jan 78]

[English abstract from source]

The experiments on an isolated frog neuromuscular preparation gave evidence that an exposure to stable magnetic fields of 1000–4000 Oe did not influence the time parameters, amplitude and pattern of the action potentials of the gastrocnemius muscle induced by ischiatic nerve stimulation with single impulses. Similar results were obtained from an analysis of electric responses of the upper cervical sympathetic node to the stimulation of preganglionar fibers in in situ experiments on urethane anesthesized rabbits subjected to a total exposure of a stable magnetic field (500–3000 Oe). In addition, an exposure to a stable magnetic field of 4000 Oe brought about a decrease of the level of depression of the action potential of muscles after conditioning tetanus.

[Text] It was previously shown that exposure to high-intensity steady magnetic fields (SMF) induces significant changes in electrical responses of various brain structures to stimulation of the sciatic nerve [1-3]. Most researchers deny that SMF influence conduction of excitation through nerve fibers [4-6].

In this work, we analyzed the electric responses of muscles and a sympathetic ganglion to orthodromal stimulation during exposure to high-intensity SMF.

Methods

In this study, we used 20 rabbits and 50 isolated preparations of the frog's sciatic nerve and gastrocnemius.

The preparation was put in a moist plexiglas chamber. The muscle functioned in the isometric mode. The experiments on rabbits were conducted using urethane anesthesia (1 g/kg in 20% solution, intravenously). We studied the superior cervical sympathetic ganglion in situ, with retention of all its connections. Bipolar silver electrodes were used to stimulate the nerves and derive bioelectric potentials. Single square-wave pulses lasting 0.5 ms were used for stimulation, and action potentials were recorded on an oscillograph. As in our previous work [1-3], we used an SP-15A electromagnet with adjustable parallel flat tips (400×300 mm in size), the south pole being on the top tip. SMF was virtually homogeneous in the central part of the interpole space (300×200 mm in size), with no more than 15-20% drop in intensity on the periphery of the field, as compared to the center. Pulsation of intensity constituted 1.8%. The magnetic force lines were perpendicular to the objects studied. The neuromuscular preparations were exposed to 1000 or 4000 Oe SMF for 10-20 min. The action potentials of the gastrocnemius, which appeared during stimulation of the sciatic nerve, were recorded before switching the electromagnet on, during exposure to SMF and for 10 min after turning the electromagnet off. The rabbits were tied to a stand with their back down; they were put in the space between poles and submitted to total-body exposure to SMF of increasing intensity: 500, 1000, 2000 and 3000 Oe. Total exposure time was 20 min. Stimulation of the cervical sympathetic nerve and recording of action potentials of the sympathetic ganglion of each rabbit were performed before exposure to SMF, during exposure and after turning the electromagnet off. Experiments of the same duration without using an electromagnetic served as a control.

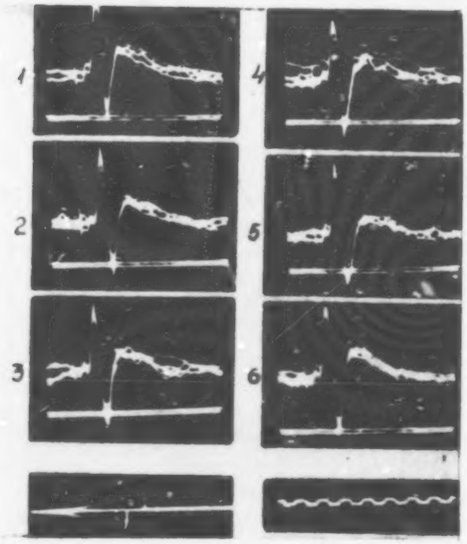

Figure 1. Effect of SMF of increasing intensity on action potential of superior cervical sympathetic ganglion of a rabbit. Calibration of intensification, 50 μV; time mark, 10 ms

1) before exposure; 2-5) SMF of 500, 1000, 2000 and 3000 Oe, respecitvely; 6) after turning off the electromagnet

Results and Discussion

As a result of our studies, we found that exposure to SMF of 1000 Oe does not alter the threshold of excitability of the frog neuromuscular preparation and does not affect the latency period and amplitude of action potential of the muscle. The fluctuations in action potential (in mV) of the muscle with exposure to 4000 Oe SMF were within the range of experimental error: 3.22±0.41 before exposure, 297±0.42 when the electromagnet was turned on, 3.22±0.45 (3 min) and 3.68±0.53 (10 min) during exposure, 3.16±0.71 during the period of turning the SMF off, and in the aftereffect period 3.38±0.56 (3 min) and 3.74±0.51 (10 min) no changes in shape of potential were demonstrable. Since we did not obtain data about the effect of SMF on transmission of excitation in a myoneural synapse and generation of action potential in the muscular effector, we tried to assess these processes in a more complex structure where interneuronal transmission of impulses was involved. The sympathetic ganglia are a convenient and widely used object for demonstration of patterns of interneuronal transmission of excitation.

The studies revealed that SMF of 500-3000 Oe did not have an appreciable effect on the latency period, amplitude and duration of action potentials of a sympathetic ganglion. Thus, while the latency period constituted 7.0±0.4, time was 76.3±2.4 ms and amplitude of potential was 115.4±38.6 μV in the background period, the figures were 7.2±0.5, 76.8±2.2 ms and 104.2±29.1 μV, respectively, after exposure to SMF of 3000 Oe.

Exposure to SMF did not have an appreciable effect on the shape of potentials of the sympathetic ganglion either. Figure 1 shows that a three-phase potential appeared upon stimulation of preganglionic fibers in the sympathetic node, and the shape and amplitude thereof remained unchanged throughout the period of exposure of a rabbit to SMF of ascending intensities. Consequently, we failed to demonstrate an influence of SMF on processes related to synaptic transmission of impulses and generation of potentials in a sympathetic node.

Even in such a complexly organized structure as a sympathetic node, which has insertion neurons and where conduction of excitation is related to multiplication of the electric signal due to synaptic contacts between one preganglionic fiber and many neurons, we did not observe exaltation of electric responses, which are readily demonstrable in brain structures, during exposure to SMF. However, we cannot apparently believe that SMF is totally neutral in relation to the function of peripheral innervation systems. Thus, SMF has a distinct influence on the course of restoration of initial bioelectrical activity after pretetanization of a neuromuscular preparation (stimulation of the nerve at a frequency of 50 Hz for 30 s). In control experiments, conditioning tetanus induced profound and prolonged depression of the electrical reaction of the muscle to test stimulation of the nerve with single pulses. This effect of tetanization was significantly attenuated during exposure to SMF. The period of posttetanic depression was shorter, and it was not present at all in a number of cases. In some of the experiments, instead of posttetanic depression there was development of posttetanic potentiation under the influence of SMF

(Figure 2). Figure 3 illustrates the results of this series of experiments. Attenuation of posttetanic depression of muscular action potential persisted for some time after turning off the electromagnet.

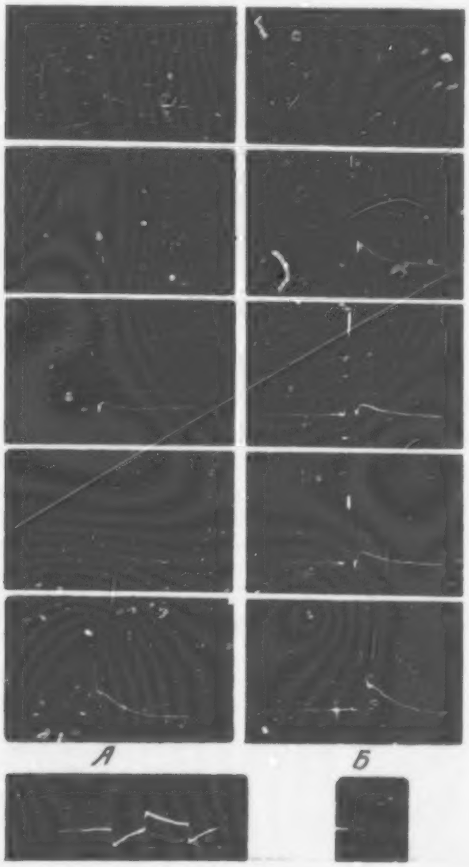

Figure 2. Posttetanic changes in action potential of the frog's gastrocnemius before (A) and during (Б) exposure to SMF of 4000 Oe. Calibration of intensification, 500 μV; time mark 5 ms.

1) before tetanization
2-5) 30 s, 2, 5 and 10 min, respectively, after tetanization

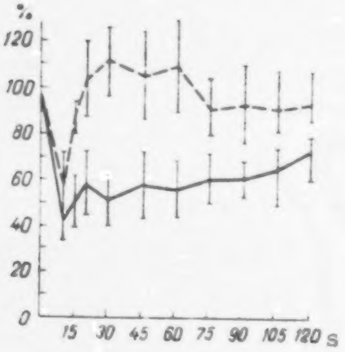

Figure 3.
Effect of SMF on degree of posttetanic depression of muscular action potential.

X-axis, time after tetanization (s); y-axis, amplitude of potential (% of initial level). Solid line, before exposure; dash line, during exposure to SMF of 4000 Oe.

The obtained data warrant the assumption that SMF, in the tested range of intensities, does not impair the mechanisms that implement synaptic transmission of single impulses and electrogenesis in the neuromuscular system and sympathetic ganglia. However, it can affect residual processes after rhythmic activation of the innervation system. In order to comprehend the mechanisms of this phenomenon, studies must be made of the processes that are related to metabolism of acetylcholine and calcium, to which an important role is attributed in the genesis of postactivation changes in synaptic transmission of impulses [7]. There are indications in the literature of changes in cholinesterase activity and behavior of calcium ions as a result of exposure to SMF [8, 9].

BIBLIOGRAPHY

1. Klimovskaya, L. D., and Smirnova, N. P. in "Vliyaniye magnitnykh poley na biologicheskiye ob"yekty. Vsesoyuznyy simpozium. 3-y. Materialy" [Proceedings of 3d All-Union Symposium on Effects of Magnetic Fields on Biological Objects], Kaliningrad, 1975, p 216.

2. Idem, BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 8, 1976, pp 906-910.

3. Smirnova, N. P., and Klimovskaya, L. D. in "International Conference on Magnet Technology," 6th, Bratislava, 1977, p 36.

4. Liberman, Ye. A.; Vantsvayg, M. N.; and Tsofina, L. M. BIOFIZIKA [Biophysics], No 4, 1959, pp 505-506.

5. Valentinuzzi, M. BULL. MATH. BIOPHYS., Vol 27, 1965, pp 203-214.

6. Abashchin, V. M. and Yevtushenko, G. I. BIOFIZIKA, No 2, 1975, pp 281-282.

7. Wilson, D. F., and Skirboll, L. R. AM. J. PHYSIOL., Vol 227, 1974, pp 92-95.

8. Young, W. in "Biological Effects of Magnetic Fields," New York, Vol 2, 1969, pp 79-102.

9. Kislovskiy, L. D., and Puchkov, V. V. in "Voprosy teorii i praktiki magnitnoy obrabotki vody i vodnykh sistem" [Problems of Theory and Practice of Magnetization of Water and Aqueous Systems], Moscow, 1971, pp 25-31.

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EFFECTS OF STRONG INFRALOW-FREQUENCY MAGNETIC FIELDS ON BONE MARROW CELL DIVISION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 6, 1979 pp 61-63

[Article by A. D. Strzhizhovskiy, G. V. Galaktionova and P. A. Cheremnykh, submitted 15 Nov 77]

[English abstract from source]

The effect of an infralow frequency magnetic field of 3–127 kOe applied for 1 hr on mitotic activity, frequency of chromosomal aberrations and number of bone marrow cells of mice was studied. The exposure of mice to fields of 3 and 8 kOe stimulated and to fields of 51 and 127 kOe inhibited mitotic activity. No increase in the frequency of aberrant mitoses in bone marrow cells was noted. The changes in the cell number were small (no more than 20%) and readily reversible.

[Text] Interest in studying the biological effects of strong magnetic fields has increased because of the possibility of using them in space flights [1, 2]. The information in the literature [2-4] was obtained primarily from experiments with steady magnetic fields, whereas virtually no studies have been made of the effects of infralow-frequency magnetic fields (IMF). In this work, we studied the effects of IMF over a wide range of intensities on division of mouse bone marrow cells.

Methods

A water-cooled electromagnetic with cylindrical active zone was used as the IMF source. The field it induced consisted of two components, one of which was constant and the other changed in accordance with the saw-tooth ["saw-like"] law, with a period of T = 30 s. The intensity of the constant component coincided with the amplitude of the saw-tooth component. Overall intensity of the IMF constituted 130 kOe in the center of the active zone, dropping to 1.4 kOe at the ends (35 cm away from the center in both directions).

Experimental mice, placed in duralumin boxes, were put in different parts of the active zone and exposed to IMF for 1 h. The direction of the IMF coincided with the animal's longitudinal body axis. During exposure, fresh air was supplied to the animals by means of forced ventilation, for which reason the temperature in the active zone of the electromagnet was virtually the same as the ambient temperature.

Experimental animals were decapitated, concurrently with controls, immediately after removal from the active zone of the electromagnetic, as well as on the 1st, 2d, 3d, 15th and 55th days, and we determined the number of karyocytes per femur, as well as incidence of aberrant mitoses at the anaphase stage (bridges and acentric fragments). The mitotic index was determined on the basis of a count of number of mitoses per 3000-5000 cells in smears fixed with methyl alcohol and stained with methylene blue. In all, we used 166 mice in the tests.

Results and Discussion

For some time after discontinuing exposure to IMF the animals were substantially less active, but none died while in the active zone of the electromagnetic or within 55 days after removal from it.

We observed stimulation of mitotic activity of bone marrow cells after discontinuing exposure to IMF of 3 and 8 kOe; however, it did not last long and disappeared within 1 day after removal of experimental animals from the active zone of the electromagnet (see Table). Thereafter, up to the end of the observation period (55th day), we failed to demonstrate reliable changes in the mitotic index. The reaction of bone marrow cells was somewhat different when exposed to IMF of superhigh intensity (54 and 127 kOe). No changes in mitotic activity were found immediately after exposure; however, it then began to decline and reached a minimum by the end of the first post-exposure day. Subsequently, there was gradual restoration of mitotic activity to the normal level. The amplitude of the effect increased with increase in IMF intensity.

The spectrum of the observed changes in mitotic activity and order in which they appeared with increase in IMF intensity were quite typical of the effects of relatively mild stimuli, which do not induce gross organic disturbances. Regardless of the specific mechanism of biological action of the stimulus, mild factors usually stimulate physiological functions and strong ones inhibit them, the intensity of the effect corresponding to a change in nature of the reaction being different for different systems and stimuli. The latter circumstance is of substantial importance to interpretation of the obtained data, since bone marrow is a heterogeneous tissue and the magnetobiological effect in question reflects the overall reaction of the different series of blast cells of bone marrow.

According to information in the literature concerning changes in composition of peripheral blood during exposure to steady magnetic fields [2, 5, 6], which apparently have a mechanism of action similar to that of IMF, the reactions of erythroid and myeloid blast elements of bone marrow are quite complex and occur in opposite directions. In rather strong fields, there is inhibition of myeloid cell proliferation, whereas erythroid cells are subject to a dual influence. In addition to direct inhibition of cell division, the magnetic field apparently induces tissue hypoxia followed by discharge into blood of erythropoietin, which stimulates proliferation of erythroid cells. The presence of reticulocytosis in peripheral blood of animals exposed to magnetic fields leads us to the conclusion that tissular hypoxia is the predominant factor. If these patterns also apply to IMF, the results of our study are indicative of the decisive role of myeloid cells in the integral reaction of mitotic activity of bone marrow.

Mitotic index (% of control) of mouse bone marrow at different times after 1-hour exposure to IMF varying in intenstiy (M±m)

Fixing day	Intensity of IMF, kOe			
	3	8	54	127
0	121.1±8.9	114.2±4.2	106.1±3.1	97,4±8,4
1	101,8±6.1	95.5±9.8	55.5±5.2	32.8±4.0
2	89,0±7,8	103,5±15.6	78,6±7.5	72,5±13,4
3	105,8±8,6	94.5±4.2	75,0±8,5	98.2±3,6
15	116,1±10,4	90,5±7.5	98.6±6,9	82,0±8,2
55	87,2±8.2	98,0±12,6	110,8±11,3	86,2±11,3

We failed to demonstrate degenerative changes in interphase bone marrow cells of mice exposed to IMF of the above-mentioned intensity and duration. The change in number of cells was not significant (no more than 20%) and readily reversible.

The incidence of chromosomal aberrations is an important criterion of integrity of genetic structures of tissular cells. We failed to demonstrate an increase in incidence of aberrant mitoses in bone marrow cells of experimental animals. However, it must be indicated that we only recorded rather gross chromosomal lesions in analyzing material in the anaphase. Consequently, we cannot rule out the possiblity of onset of finer genetic effects and related long-term sequelae of exposure to IMF.

BIBLIOGRAPHY

1. Trukhanova, K. A.; Ryabova, T. Ya.; and Morozov, D. Kh. "Active Protection of Spacecraft," Moscow, Atomizdat, 1970.

2. Busby, D. E. SPACE LIFE SCI., Vol 1, 1968, pp 23-63.

3. Vilenchik, M. M. USPEKHI SOVR. BIOL. [Advances in Modern Biology], Vol 63, No 1, 1967, pp 54-72.

4. Nakhil'nitskaya, Z. N. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1974, pp 3-15.

5. Borodkina, A. G. Ibid, No 1, 1976, pp 66-70.

6. Piruzyan, L. A.; Glezer, V. M.; Lomonosov, V. A.; et al. IZV. AN SSSR. SER. BIOL. [News of the USSR Academy of Sciences, Biology Series], No 1, 1972, pp 142-145.

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PROGRAMMED CONTROL OF THE AUTOTROPHIC COMPONENT OF AN ECOLOGICAL SYSTEM THAT IS CLOSED WITH REGARD TO EXCHANGE OF GASES

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No 6, 1979 pp 63-68

[Article by A. S. Nasonov and V. S. Toroptsov, submitted 3 May 77]

[English abstract from source]

The ecological system with closed gas exchange consisting of autotrophic and heterotrophic components located in different rooms was studied. The conditions of O_2 and CO_2 steady state with a periodically working autotrophic component were found. The stability of the steady state was analyzed.

[Text] There have been studies of stability [steady state] of O_2 and CO_2 in the atmosphere of a closed ecological system consisting of an autotrophic component (photosynthesizing microalgae) and heterotrophic component in the same compartment [1, 2]. The possibility, in principle, of designing temporary [or time-related] programmed control of two modes of function of the atuotrophic component has been demonstrated.

Our objective here was to discuss programmed control for the more general case, when heterotrophic components are present in several compartments [rooms, spaces] simultaneously. Recommendations are offered on the choice of parameters for programmed control that implements stable periodic changes in concentrations of O_2 and CO_2 around the mean levels in each compartment.

The values of the O_2 and CO_2 concentrations in the compartments should remain within a rather narrow, specified, permissible range [3]. The duration of modes of function of the autotrophic component must be short, so that the concentrations of O_2 and CO_2 would not exceed this range in the course of periodic changes.

The dynamic model of gas exchange discussed here has been designed with due consideration of previously developed models of autotrophic and heterotrophic components [2].

Description of Model

Let the heterotrophic components be present simultaneously in several compartments whose volumes are W_i $(i = 1, \overline{n})$. The autotrophic component regenerates the gas environment in the compartments, while the heterotrophic components take up O_2 and discharge CO_2. The volumetric rates of O_2 uptake and CO_2 output by the heterotrophic components equal V_{x_i} and V_{y_i}, respectively, and they are usually considered constant in calculations [2].

The gas mixture is collected from the habitable compartments with concentrations x_i of oxygen and y_i of carbon dioxide into a common collector and pumped through a system of microalgae cultivation at a volumetric rate coming in contact with the cell suspension. As a result of photosynthesis, there is partial absorption of CO_2 and discharge of O_2 from the gas mixture with concentration x of oxygen and y of carbon dioxide. The intensity of photosynthesis depends on intensity of light in the bioculture apparatus and concentration y of carbon dioxide in the gas mixture, but not on the concentration x of oxygen. The autotrophic component (photosynthesizing microalgae) function in two modes I_1 and I_2: in mode I_1 the intensity of illumination provides for regeneration of incoming gas mixture with a certain reserve, whereas in mode I_2, on the contrary, it does not (the second mode could also be called the dark mode, when the intensity of illumination of the bioculture device equals zero). Let us use τ_1 to designate duration of function of the autotrophic component in mode I_1 and τ_2 to designate this in mode I_2. Then the sum of $\tau_1 + \tau_2$ will be the duration of the functional cycle T_c of the closed ecological system.

Let us use $V_y^{01}(y)$ to refer to volumetric rate of CO_2 uptake in mode I_1 and $V_y^{02}(y)$ for the rate in mode I_2, and $V_x^{01}(y)$ and $V_x^{02}(y)$ to designate the corresponding volumetric rates of O_2 discharge.

In the light-containing modes, functions $V_y^{01}(y)$, $V_y^{02}(y)$, $V_x^{01}(y)$ and $V_x^{02}(y)$ increase monotonously.

The flow of gas, partially cleared of CO_2 and enriched with O_2, is distributed in a specific proportion $\omega_i (0 \leq \omega_i \leq 1)$ in the habitable compartments, and

$$\sum_{i=1}^{n} \omega_i = 1.$$

Steady State Conditions

Let us consider changes in concentrations of O_2 and CO_2 in habitable compartments.

Let the concentrations of O_2 equal $x_i(t) (i = 1, \overline{n})$ and CO_2 equal $y_i(t)$ $(i = 1, \overline{n})$ at time t. Within the cycle T_c, they will present the following increments: $\Delta x_i(t) = x_i(t+T_c) - x_i(t)$ and $\Delta y_i(t) = y_i(t+T_c) - y_i(t)$.

The ratios $\Delta x_i(t)/T_c$ and $\Delta y_i(t)/T_c$ express the mean rates of change in concentration of O_2 and CO_2, respectively, in the ith compartment within interval T_c. In view of the above hypotheses concerning the short duration of the work cycle T_c for the autotrophic component, the changes in concentration of O_2 and CO_2 in habitable compartments can be described rather accurately by the following system of differential equations:

$$\frac{d\bar{x}_i}{dt} = \frac{1}{W_i}\{\omega_i[Q(\bar{x} - \bar{x}_i) + \bar{V}_x(\bar{y})] - V_{x_i}\}, \tag{1a}$$

$$\frac{d\bar{y}_i}{dt} = -\frac{1}{W_i}\{\omega_i[Q(\bar{y} - \bar{y}_i) - \bar{V}_y(\bar{y})] + V_{y_i}\} \tag{1b}$$

where $\bar{x}_i$ is mean O_2 concentration in ith compartment; $\bar{x} = \sum_{i=1}^{n}\omega_i\bar{x}_i$ is mean is mean concentration of O_2 in collector gas mixture; $\bar{y}_i$ is mean concentration of CO_2 in ith compartment; $\bar{y} = \sum_{i=1}^{n}\omega_i\bar{y}_i$ is the mean concentration of CO_2 in collector gas mixture; $\bar{V}_x(\bar{y}) = \dfrac{V_x^{01}(\bar{y})\cdot\tau_1 + V_x^{02}(\bar{y})\cdot\tau_2}{T_c}$ is mean volumetric rate of O_2 output by autotrophic component within the period of the cycle; $\bar{V}_y(\bar{y}) = \dfrac{V_y^{01}(\bar{y})\cdot\tau_1 + V_y^{02}(\bar{y})\cdot\tau_2}{T_c}$ is the mean volumetric rate of CO_2 uptake by the autotrophic component within the cycle.

The integral curves $\bar{x}_i(t)$ and $\bar{y}_i(t)$ physically characterize the changes in the smoothed (mean) values of concentrations of O_2 and CO_2 in the corresponding compartments in time, near which there are changes in their true values $x_i(t)$ and $y_i(t)$ during periodic alternation of modes of function of the autotrophic component.

Apparently, one should select a program for duration of operation of the autotrophic component, τ_1 and τ_2 in each of modes I_1 and I_2, from the condition of steady state of the closed ecosystem [1]:

$$\bar{V}_x(\bar{y}) = \sum_{i=1}^{n} V_{x_i}; \tag{2a}$$

$$\bar{V}_y(\bar{y}) = \sum_{i=1}^{n} V_{y_i} \tag{2b}$$

or, for each habitable compartment:

$$\begin{cases} \omega_i[Q(\bar{x} - \bar{x}_i) + V_x(\bar{y})] = V_{x_i}; & \text{(3a)} \\ \omega_i[Q(\bar{y} - \bar{y}_i) - V_y(\bar{y})] = -V_{y_i}. & \text{(3b)} \\ i = \overline{1, n} & \end{cases}$$

Conditions of Stability

To analyze the stability of a closed ecological system for CO_2, it is sufficient to merely consider equation (1b), since the rate of change in concentration of CO_2 is unrelated to concentration of O_2.

Let the concentration of CO_2 deviate from steady values $\tilde{y}_i$ by a value of $\bar{y}_i$.

Then, according to equation (1b), we shall have:

$$\frac{d(\bar{y}_i + \Delta\bar{y}_i)}{dt} = \frac{1}{W_i}\{\omega_i[Q(\bar{y} + \Delta\bar{y} - (\bar{y}_i + \Delta\bar{y}_i)) - \bar{V}(\bar{y} + \Delta\bar{y})] + V_{y_i}\}$$

Hence:

$$\frac{d\Delta\bar{y}_i}{dt} = \frac{\omega_i}{W_i}[Q(\Delta\bar{y} - \Delta\bar{y}_i) + \bar{V}_y(\bar{y}) - \bar{V}_y(\bar{y} + \Delta\bar{y})]. \qquad (4)$$

where

$$\Delta\bar{y} = \sum_{i=1}^{n} \omega_i \cdot \Delta\bar{y}_i.$$

Let us insert the function of Lyapunov:

$$F^y = \frac{1}{2Q} \cdot \sum_{i=1}^{n} \Delta\bar{y}_i^2 \cdot W_i. \qquad (5)$$

The derivative of function F^y according to time can be written down as:

$$\dot{F}^y = \Delta\bar{y}^2 - \sum_{i=1}^{n} \omega_i \cdot \Delta\bar{y}_i^2 + \frac{\bar{V}_y(\bar{y}) - V_y(\bar{y} + \Delta\bar{y})}{Q} \cdot \Delta\bar{y}. \qquad (6)$$

Let us separate the last equation into two parts:

$$\dot{F}_1^y = \Delta\bar{y}^2 - \sum_{i=1}^{n} \omega_i \cdot \Delta\bar{y}_i^2$$

and

$$\dot{F}_2^y = \frac{\bar{V}_y(\bar{y}) - \bar{V}(\bar{y} + \Delta\bar{y})}{Q} \cdot \Delta\bar{y}.$$

Let us examine each of them separately.
First, let us consider the quadratic form:

$$\dot{F}_1^y = \Delta\bar{y}^2 - \sum_{i=1}^{n} \omega_i \cdot \Delta\bar{y}_i^2 = \left(\sum_{i=1}^{n} \omega_i \cdot \Delta y_i^2\right)^2 - \sum_{i=1}^{n} \omega_i \cdot \Delta\bar{y}_i^2. \qquad (7)$$

Let us determine its sign with different values of n.
Let us assume that $n = 1$. In this case, $\omega_1 = 1$ and $\dot{F}_1^y = 0$.
Let $n = 2$. Then:

$$\dot{F}_1^y = \sum_{i=1}^{n} \omega_i \cdot (\omega_i - 1) \cdot \Delta\bar{y}_i^2 + 2\omega_1 \cdot \omega_2 \cdot \Delta\bar{y}_1 \cdot \Delta\bar{y}_2. \qquad (8)$$

If we were to use the equation $\sum_{i=1}^{n}\omega_j = 1$, the formula for $\dot{F}_1^y$ with $n = 2$ could easily be reduced to the following form:

$$\dot{F}_1^y = -\omega_1 \cdot \omega_2 \cdot (\Delta\bar{y}_1 \Delta\bar{y}_2)^2. \qquad (9)$$

Hence, form (9) is determined negatively.

Let us consider the case when $n>2$.

After submitting formula (7) to a series of transformations, we shall obtain:

$$\begin{aligned} F_1^y = {} & \omega_1 \cdot (\omega_1 - 1) \cdot \Delta\bar{y}_1^2 + \omega_1 \cdot \omega_2 \cdot \Delta\bar{y}_1 \cdot \Delta\bar{y}_2 + \ldots + \omega_1 \cdot \omega_n \cdot \Delta\bar{y}_1 \cdot \Delta\bar{y}_2 + \\ & + \omega_2 \cdot \omega_1 \cdot \Delta\bar{y}_2 \cdot \Delta y_1 + \omega_2 \cdot (\omega_2 - 1) \cdot \Delta\bar{y}_2^2 + \ldots + \omega_2 \cdot \omega_n \cdot \Delta\bar{y}_2 \cdot \Delta\bar{y}_n + \\ & + \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots + \\ & + \omega_n \cdot \omega_1 \cdot \Delta\bar{y}_n \cdot \Delta y_1 + \omega_n \cdot \omega_2 \cdot \Delta\bar{y}_n \cdot \Delta\bar{y}_2 + \ldots + \omega_n \cdot (\omega_n - 1) \cdot \Delta\bar{y}_n^2. \end{aligned}$$

In order to define the negativity of the quadratic form of F_1^y it is enough to comply with the conditions [4]: $\Delta_1<0,\ \Delta_2>0,\ \Delta_3<0, \ldots,$

and

$$\Delta_m = \prod_{k=1}^{m} \omega_k \cdot \Delta_m^1 \quad (m = \overline{1,n}),$$

where

$$\left.\begin{aligned} & \Delta_1' = \omega_1 - 1 \\ & \Delta_2' = 1 - \omega_1 - \omega_2; \\ & \Delta_m' = (m-2)! \cdot \sum_{\substack{j=1 \\ l=2}}^{m} \Delta_{jl} \cdot \prod_{i=1}^{m} (\omega_i - 1); \\ & l > j;\ i \neq j;\ i \neq l;\ m = \overline{3,n}; \end{aligned}\right\} \tag{10}$$

$$\Delta_{jl} = \begin{vmatrix} \omega_j - 1 & \omega_l \\ \omega_j & \omega_l - 1 \end{vmatrix}. \tag{11}$$

Hence:

$$\left.\begin{aligned} & \Delta_1 < 0; \\ & \Delta_2 > 0; \\ & \Delta_{jl} = 1 - \omega_j - \omega_l > 0 \end{aligned}\right\}. \tag{12}$$

Since, with $n>2$ $\omega_i<1$, the products $\prod\limits_{i=1}^{m} (\omega_i - 1)$ and,

consequently, determinants $\Delta'_m<0$ with an uneven m, and they are greater than zero with even m.

Thus, $\Delta'_1<0$, $\Delta'_2>0$, $\Delta'_3<0, \ldots$, and the quadratic form of $\dot{F}_1^y$ with $n>2$ is negatively determined.

Consequently, $\dot{F}^y_{\_} \equiv 0$ with $n = 1$ and $\dot{F}_1^y<0$ with $n \geq 2$.

Let us return to the second part of formula (6). Let us consider the form of $\dot{F}_2^y$.

In view of the nature of change in functions $\bar{V}_y(\bar{y})$, we shall have:

$$\bar{V}_y(\bar{y}+\Delta\bar{y}) > \bar{V}_y(\bar{y}) \text{ with } \Delta\bar{y} > 0 \text{ and}$$
$$\bar{V}_y(\bar{y}+\Delta\bar{y}) < \bar{V}_y(\bar{y}) \text{ with } \Delta\bar{y} < 0.$$

It can be concluded from this that function $\dot{F}_2^y$ is also negatively defined and, consequently, the concentration of CO_2 in each of the compartments will come asymptotically close to its stationary values.

Now let us analyze stability according to O_2 concentration.

We obtain from equation (1a), with consideration of steady state condition (3a):

$$\frac{d\Delta\bar{x}_i}{dt} = \frac{\omega_i}{W_i}\left[Q\left(\Delta\bar{x}-\Delta x_i\right)+\bar{V}_x(\bar{y}+\Delta\bar{y})-\bar{V}_x(\bar{y})\right], \qquad (13)$$

where $\quad i=\overline{1,n}$

$$\Delta\bar{x} = \sum_{i=1}^{n} \omega_i \cdot \Delta\bar{x}_i.$$

Let us consider the function of Lyapunov:

$$F^x = \frac{1}{2Q}\sum_{i=1}^{n}\left(\Delta\bar{x}_i^2+\Delta\bar{y}_i^2\right)\cdot W_i \qquad (14)$$

and its derivative:

$$\dot{F}^x = \Delta\bar{x}^2 - \sum_{i=1}^{n}\omega_i\cdot\Delta\bar{x}_i^2 + \frac{\bar{V}_x(\bar{y}+\Delta\bar{y})-\bar{V}_x(\bar{y})}{Q}\cdot\Delta\bar{x} + \dot{F}^y. \qquad (15)$$

To analyze the sign of form $\dot{F}^x$, let us break down the last equation into three components, $\dot{F}_1^x$, $\dot{F}_2^x$ and $\dot{F}_3^x = \dot{F}^y$, where:

$$\dot{F}_1^x = \Delta\bar{x}^2 - \sum_{i=1}^{n}\omega_i\cdot\Delta\bar{x}_i^2;$$

$$\dot{F}_2^x = \frac{\bar{V}_x(y+\Delta\bar{y})-\bar{V}_x(y)}{Q}\cdot\Delta\bar{x}.$$

For quadratic form (9), which coincides with the quadratic form $\dot{F}_1^x$ with accuracy up to the notations, it was shown that with $n>1$ it is negatively defined and with $n = 1$ it equals zero. Further, acccording to the physical essence of the phenomena that take place in the autotrophic component, product $\Delta\bar{y}(t)\cdot\Delta\bar{x}(t)$ is always negative [2]. For this reason, in view of the initial premises concerning the form of functions $V_x^{01}(y)$ and $V_x^{02}(y)$, we shall have $\dot{F}_2^x<0$ with $\Delta\bar{x} \neq 0$ and $\dot{F}_2^x = 0$ with $\Delta\bar{x} = 0$.

Finally, we have demonstrated above that function $\dot{F}^y = \dot{F}_3^x$ is definitely negative. Consequently, the concentration of O_2 in any of the compartments will asymptotically approach the position of equilibrium [4].

Thus, if the parameters of programmed control τ_1 and τ_2 are selected from the conditions of equations (2) or (3), there will be stable periodic changes, in a closed ecosystem, in concentrations of O_2 and CO_2 in the vicinity of certain mean levels in each compartment.

BIBLIOGRAPHY

1. Shabel'nikov, V. G. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1975, pp 10-13.

2. Idem, Ibid, No 6, pp 36-40.

3. Smirnov, I. V. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 19, 1972, pp 90-180.

4. Merkin, D. R. "Introduction Into Theory of Steadiness [Stability] of Movement," Moscow, 1976.

BRIEF REPORTS

UDC: 612.273.2.014.41

ANIMAL RESISTANCE TO HYPOXIA UNDER HYPERBARIC CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 68-69

[Article by Yu. I. Zakharov and V. V. Isayenko, submitted 26 Dec 78]

[Text] We were able to find only one work in the literature that deals with direct investigation of animal resistance to hypoxia under hyperbaric conditions [1]. The author demonstrated that white mouse survival time was longer under high pressure (6 kgf/cm^2) and hypoxia (4.2% oxygen in nitrogen) than for animals exposed to an analogous gas environment at atmospheric pressure. To explain this phenomenon, the cited author assumes that the nitrogen anesthesia that occurs at a pressure of 6 kgf/cm^2 leads to a decline of intensity of metabolic processes in the central nervous system, thereby protecting the central nervous system against the effect of hypoxia.

We have tried to determine here the extent to which the results in [1] can be extended to other animal species and other experimental conditions.

Methods

We conducted our study on 111 mongrel, male albino rats weighing 160-200 g. The control group (48 animals) was kept in a hypoxic environment (pO_2 40 mm Hg in nitrogen of extreme purity) at a pressure of 1 kgf/cm^2. The experimental group (63 animals) was kept in the same gas environment at a pressure of 6 kgf/cm^2. Carbon dioxide was absorbed by means of a lime [or calcium] absorber. The composition of the gas environment was monitored constantly with a Beckman OM-11 oxygen analyzer. The required pO_2 was obtained by diluting atmospheric air with extremely pure nitrogen. Along with dilution of the air with nitrogen, the pressure was raised in the experimental group. The time required to establish operating conditions constituted 14±0.2 min for the control group and 15±0.8 min for the experimental one. We counted survival time from the moment the specified conditions were reached.

Temperature fluctuations were reduced to a minimum by means of a thermostat system. Only brief temperature fluctuations in the range of 21-24°C were noted during compression.

The experimental and control animals were under continuous observation. We recorded the time they assumed a lateral position and that of respiratory arrest. In some cases (1 rat out of every 5-6 in the pressure chamber) we also recorded respiration rate by means of a carbon sensor and measured rectal temperature.

Results and Discussion

At normal pressure, the animals assumed a lateral position in 59.1±5.3 min and at 6 kgf/cm^2 they did so in 8.1±1.7 min ($P<0.01$). Survival time constituted 89.1±1.3 min in the control and 20.3±1.2 min at high pressure (according to respiratory arrest; $P<0.01$).

At the moment of respiratory arrest, body temperature was 36.8±0.2°C, and it was reliably higher ($P<0.01$) than in the control group (34.4±0.14°C); however, the difference in body temperature should be interpreted as the result of differences in survival time, rather than the cause of these differences.

The obtained data indicate that high barometric pressure diminishes animal survival time with exposure to hypoxia. This phenomenon can be explained by the substantial breathing difficulty under hyperbaric conditions, which is aggravated by hypoxia, in the presence of which pulmonary ventilation should increase significantly.

We cannot explain the reasons for the difference between the results we obtained and the data obtained in the study on mice [1]. Perhaps, this difference can be attrbitued to the fact that rats are less susceptible to nitrogen anesthesia than mice.

BIBLIOGRAPHY

1. Hogberg, T., and Soderberg, U. ACTA ANAESTH. SCAND., Vol 17, 1973, pp 159-162.

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EFFECT OF CARBON MONOXIDE ON ANIMALS ADAPTED TO HYPOXIC HYPOXIA

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No 6, 1979 pp 69-72

[Article by V. V. Kustov and V. G. Litau, submitted 17 May 77]

[Text] It has now been established that preadaptation of animals to hypoxic hypoxia enahnces their resistance to the toxic effect of carbon monoxide [1, 2].

However, there are no data in the literature concerning development of carbon monoxide poisoning in animals adapted to hypoxic hypoxia.

This study deals with the above question.

Methods

Experiments were conducted on 80 white male mice initially weighing 24-26 g. The animals were divided into 4 groups of 20 mice in each. The first group of mice was adpated to hypoxia as follows: they were kept for 4 h in the pressure chamber, at an "altitude" of 1000 m, on the first day; the "altitude" was increased to 4000 m on the 2d day, to 5000 m on the 3d day, to 5500 m on the 4th and to 6000 m on the 6th day. For the next 3 months, the animals were kept at this altitude for 4 h a day, 5 times a week. The second group of mice was conditioned to hypoxia as described above, and together with the animals of the third group they were exposed to carbon monoxide for 2 h a day, 5 times a week, for 3 months. We used a concentration of carbon monoxide (500±10 mg/m^3) that caused development of distinction functional disturbances of several organs and systems of experimental mice upon repeated exposure [3]. The fourth group of animals was the control.

We studied the following parameters: body weight, hemoglobin and erythrocyte content of peripheral blood, blood catalase activity, blood peroxidase activity [4] and increment of carboxyhemoglobin [5].

Table 1. Some hematological and biochemical parameters of white mice exposed to carbon monoxide during adaptation to hypoxia

Parameter	Mouse group	Day of experiment					
		before exper.	10	20	40	60	90
Hemoglobin, g/ℓ	1	108±1,0	103±2,6	119±7,0*	113±5,0	112±4,0	108±2,9
	2	105±7,0	108±7,0	127±5,0*	122±2,0*	135±1,0*	115±2,0
	3	110±2,0	106±5,0	114±2,0	116±2,0	111±5,0	88±4,0*
	4	110±1,0	110±7,0	113±7,0	109±1,0	98±6,8	100±1,0
Erythrocytes, millions/μℓ	1	10,0±0,4	9,65±0,3	9,83±0,1	9,92±0,1	10,2±0,1	10,1±0,2
	2	10,1±0,2	9,86±0,1	9,98±0,3	10,1±0,1	10,2±0,06	10,1±0,3
	3	9,72±0,6	9,9±0,08	10,1±0,04	9,95±0,1	9,5±0,04	8,7±0,4*
	4	10,1±0,1	9,76±0,2	9,97±0,1	9,96±0,08	9,91±0,1	9,85±0,1
Blood catalase index	1	0,54±0,03	0,55±0,02	0,68±0,02*	0,60±0,03*	0,54±0,03	0,58±0,02
	2	0,57±0,05	0,57±0,02	0,61±0,04	0,69±0,06*	0,66±0,03*	0,71±0,02*
	3	0,55±0,06	0,55±0,03	0,63±0,02*	0,66±0,08*	0,54±0,03	0,57±0,03
	4	0,53±0,05	0,52±0,03	0,56±0,02	0,48±0,02	0,55±0,02	0,57±0,03
Blood peroxidase, $1 \cdot 10^{-3}$ μmole/min mℓ	1	126,3±2,7	122,4±4,6	142,8±7,4*	193,3±9,5*	137,1±3,2	132,3±3,7
	2	131,1±7,0	130,2±4,7	132,9±6,0	120,9±6,8	141,9±6,4	107,6±3,2*
	3	125,7±3,2	128,0±2,0	85,7±9,6*	142,8±1,9*	132,6±6,0	66,6±3,2*
	4	133,9±9,2	136,6±1,6	128,5±7,2	124,7±1,9	136,1±5,1	141,9±1,4

*$P<0.05$, as compared to control (4th group).

We assessed adaptation to hypoxic hypoxia according to increase in altitude ceiling (maximum "altitude" in pressure chamber, at which the mice developed seizures). Upon determination of the ceiling, each mouse was lifted to an "altitude" of 5000 m in 1 min, then each subsequent 1000 m at the rate of 1000 m/min.

Results and Discussion

The results of our study revealed that carbon monoxide in a concentration of 500±10 mg/m^2 caused a lag in weight gain by the 35th experimental day in the third group of mice, as compared to animals in the first and second groups. Thus, while the third group of mice showed a gain at this time of 2% of the base weight, the weight gain for animals in the first and second groups constituted 5 and 12%, respectively. By the end of the experiment (90th day), the difference between these groups in weight gain was more marked (7, 19 and 25%, respectively, versus 18% in the fourth group).

Table 1 lists data on hemoglobin and erythrocyte content of peripheral blood, as well as catalase and peroxidase activity.

Table 1 shows that adaptation to hypoxia led to an increase in hemoglobin content in mice of the first and second groups; this parameter underwent, on the contrary, a substantial drop in the third group of animals at the end of the experiment.

A decrease in erythrocyte count by the third month of exposure to CO was demonstrated only in the third group.

The catalase index was higher on the 20th-40th experimental days in animals of the 1st-3d groups than in the control. This parameter remained high on the 60th-90th days only in the 2d group; it did not exceed the initial level in the 1st and 3d groups. Exposure of animals to CO (3d group) induced phasic changes in blood peroxidase activity. In mice exposed to CO during the period of conditioning for hypoxia (2d group), the activity of this enzyme dropped only at the end of the experiment.

Table 2 lists data on increment of carboxyhemoglobin (COHb) in the blood of mice exposed on CO on the 1st, 60th and 90th experimental days.

Table 2. Increment of carboxyhemoglobin in blood of mice exposed to CO at different stages of the experiment

Animal group	Day of experiment		
	1	60	90
1	0	3,0±1,8	3,1±0,9
2	24,5±0,9	33,1±2,2*	30,8±2,0*
3	25,4±0,8	25,0±1,5	23,8±3,9

*Difference between 2d and 3d groups is reliable ($P<0.05$).

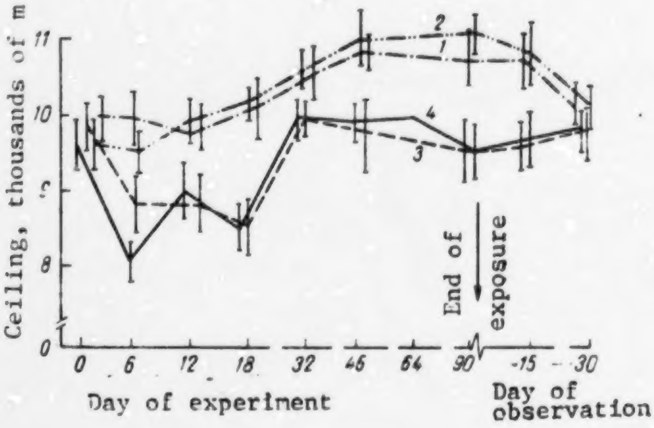
According to Table 2, there was about the same elevation of COHb level in the 3d group of mice after 2 h of exposure to carbon monoxide (500 ± 10 mg/m^3) (by a mean of 25%). The same COHb increment was recorded in the 2d groups of animals after the first exposure to carbon monoxide. However, under analogous exposure to carbon monoxide, COHb increment on the 60th and 90th experimental days was reliably higher in the 2d group than in the 3d. A slight increase in COHb content was demonstrated at these times in mice conditioned for hypoxia (1st group). This finding enables us to attribute the greater increment of COHb in the blood of mice in the 2d group (as compared to the 3d) not only to some increase in pulmonary ventilation volume under the influence of repeated exposure to hypoxia and relatively greater intake of CO, but increased formation of endogenous carbon monoxide during adaptation to hypoxic hypoxia [6].

All of the foregoing confirms the data in the literature [6], to the effect that exposure to carbon monoxide in a concentration of 500 mg/m^3 induces substantial changes in mice referable to several integral (body weight), hematological and enzymatic parameters, which are inherent in chronic carbon monoxide poisoning.

In addition, the results of our experiments indicate that the abovementioned signs of poisoning are virtually lacking in mice analogously exposed to carbon monoxide during adaptation to hypoxia, although they presented a higher COHb level after each exposure than mice exposed only to CO.

Hence, it can be concluded that adaptation of animals to hypoxia retards development of chronic CO poisoning.

The Figure illustrates the influence of the factors studied on animal adaptation to hypoxic hypoxia. As can be seen, with a 6-day interval between ceiling readings for intact animals (4th group), the ceiling did not reach its base level at each of the subsequent tested times. Total restoration of this parameter and, consequently, of changes in the body induced by establishment thereof, occurred only when the interval between readings was increased to 14 or more days. In the 1st group of animals, there was virtually no change in altitude ceiling, in the case of 6-day intervals between recordings.



Altitude ceiling for mice adapted to hypoxia.

1) conditioning for hypoxia
2) exposure to CO + adaptation to hypoxia
3) carbon monoxide alone
4) control

This fact may indicate that conditioning for hypoxia attenuates, to some extent, the adverse effect of each successive exposure to the extreme factor (determination of ceiling once every 6 days).

The dynamics of changes in ceiling for the 3d group of mice were analogous to the 4th group. A similar adaptive reaction to acute hypoxic hypoxia was observed at all experimental times in the 1st and 2d groups of mice.

On this basis, it may be concluded that repeated exposure to carbon monoxide in a concentration of 500±10 mg/m^3 did not have a substantial effect on either the reaction to acute hypoxic hypoxia or development of the set of nonspecific and specific adaptive reactions involved in animal adaptation to chronic hypoxia.

BIBLIOGRAPHY

1. Tiunov, L. A.; Vasil'yev, G. A.; and Ostapenko, O. F. in "Konferentsiya po probleme adaptatsii, trenirovki i drugim sposobam povysheniya ustoychivosti organizma. Materialy" [Proceedings of Conference on the Problem of Adaptation, Conditioning and Other Means of Enhancing Constitutional Resistance], Donetsk, 1960, p 140.

2. Vasil'yev, G. A.; Tiunov, L. A.; and Kustov, V. V. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 16, 1971, pp 178-182.

3. Tiunov, L. A., and Kustov, V. V. "Toxicology of Carbon Monoxide," Leningrad, 1969.

4. Popov, T., and Neykovska, L. GIG. I SAN. [Hygiene and Sanitation], No 10, 1971, pp 89-91.

5. Balakhovskiy, I. S.: Virovets, O. A.; and Kiselev, R. K. LABOR. DELO [Laboratory Record], No 5, 1973, pp 274-279.

6. Kolosova, T. S., and Tiunov, L. A. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1973, pp 17-21.

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EFFECT OF STEADY MAGNETIC FIELD ON SOME ASPECTS OF ENERGY AND NITROGEN METABOLISM IN THE RAT CEREBRAL HEMISPHERES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 6, 1979 pp 72-74

[Article by Ye. A. Nosova and L. M. Kurkina, submitted 28 Feb 78]

[Text] There is only fragmentary information concerning the effects of steady magnetic fields (SMF) on metabolism [1-3].

Since SMF affect central nervous system functions [4-6], we undertook a study of the effects of high-intensity SMF on ammonia, glutamine, glutamic, aspratic and gamma-aminobutyric [GABA] acids, as well as concentration of adenisine triphosphoric acid (ATP), phosphocreatine and lactic acid in the cerebral hemispheres of rats.

Methods

Experiments were conducted on male mongrel rats weighing 160-230 g. The animals were placed in a plexiglas box, 28×16×8 cm in size, with holes in the sides for ventilation, and put in an SMF of 3000 Oe for 3 h. We used an SP-15 electromagnet, the characteristics of which have been described in detail previously [13]. Upon termination of exposure, the rats were taken out of the box. The rats were frozen in liquid nitrogen 1-7 min after exposure to SMF. Control animals were maintained under the same conditions for 3 h, but without exposure to SMF.

We ground the cerebral hemispheres in a mortar with liquid nitrogen. An alcohol-water extract was obtained from frozen tissue, and determination was made of ammonia in it by the phenol-hypochlorite method [7], as well as glutamine [8] and free amino acids by the method of electrophoresis on paper [9]. In a trichloroacetic extract, we assayed ATP by column chromatography [10], phosphocreatine [11] and lactic acid [12].

Results and Discussion

Exposure of animals to SMF of 3000 Oe for 3 h did not lead to reliable changes in levels of components of the glutamine-glutamic acid system, or in aspartic acid and GABA (Table 1).

Table 1. Levels (in μM per gram wet tissue) of ammonia, glutamine and free amino acids in tissue of cerebral hemispheres after exposing rats to SMF of 3000 Oe for 3 h

Rat group	Statistical index	Ammonia	Glutamine	Glutamic acid	Aspartic acid	GABA
Control	$M \pm m$	0,40±0,03	6,33±0,19	11,01±0,52	3,51±0,13	2,55±0,12
	n	7	7	9	9	9
Experimental	$M \pm m$	0,37±0,04	6,31±0,17	10,40±0,31	3,27±0,08	2,71±0,13
	n	9	10	11	11	11

The data we obtained indicate that there are no changes in the tested nitrogen compounds, and this is inconsistent with the data of A. B. Kogan and G. V. Shcherbakova [2], who demonstrated changes in these compounds of rat brain tissue under the influence of SMF of 500 Oe. It may be assumed that these differences are attributable to differences in experimental conditions.

ATP content of brain tissue of rats exposed to SMF was reliably, though not markedly, decreased; phosphocreatine was unchanged, while lactic acid content was significantly increased (Table 2). It should be noted that ATP and lactic acid content of the rat brain did not exceed the normal range after exposure to SMF: ATP constituted 1.9-2.2 μM per gram tissue and lactic acid was 1.1-2.7 μM.

Table 2. Levels (in μM per gram wet tissue) of ATP, phosphocreatine and lactic acid in rat brain tissue after exposure to SMF of 3000 Oe for 3 h

Rat group	Statistical index	ATP	Phosphocreatine	Lactic acid
Control	$M \pm m$	2,15±0,09	2,67±0,24	1,35±0.23
	n	5	5	7
Experimental	$M \pm m$	1,89±0.05*	2,79±0,24	2,24±0,26*
	n	5	6	5

* $P<0{,}05$.

The decrease we demonstrated in ATP content of the cerebral hemispheres to the bottom range of normal and increase in lactic acid to the top range of normal are indicative of greater activity of metabolic processes in the central nervous system of rats exposed to SMF of 3000 Oe for 3 h, as compared to control animals.

BIBLIOGRAPHY

1. Shinkevich, L. L., and Shishlo, M. A. in "Soveshchaniye po izucheniyu vliyaniya magnitnykh poley na biologicheskiye ob"yekty. Tezisy dokladov" [Summaries of Papers Delivered at Conference on the Study of Effects of Magnetic Fields on Biological Objects], Moscow, 1966, pp 85-87.

2. Kogan, A. B., and Shcherbakova, G. V. Ibid, pp 39-40.

3. Savchuk, N.; Savchuk, O.; and Krutogolova, T. in "Vsesoyuznoye soveshchaniye po izucheniyu vliyaniya magnitnykh poley na biologi biologicheskiye ob"yekty. 2-ye. Materialy" [Proceedings of Second All-Union Conference on the Effects of Magnetic Fields on Biological Objects], Moscow, 1969, pp 194-196.

4. Kholodov, Yu. A. "Effects of Electromagnetic and Magnetic Fields on the Central Nervous System," Moscow, 1966.

5. Klimovskaya, L. D., and Smirnova, N. P. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 8, 1976, pp 906-910.

6. Smirnova, N. P., and Klimovskaya, L. D. ZH. VYSSH. NERVN. DEYAT. [Journal of Higher Nervous Activity], No 2, 1976, pp 403-410.

7. Kolb, V. G., and Kamyshnikov, V. S. "Clinical Biochemistry," Minsk, 1976, pp 44-45.

8. Silakova, A. I.; Trush, G. P.; and Yavilyakova, A. VOPR. MED. KHIMII [Problems of Medical Chemistry], No 5, 1962, pp 538-544.

9. Dose, K. BIOCHEM. Z., Vol 329, 1957, pp 416-421.

10. Panteleyeva, N. S., and Korotkin, Yu. S. DOKL. AN SSSR [Reports of the USSR Academy of Sciences], Vol 167, No 6, 1966, pp 1389-1392.

11. Ennor, A. H., and Rosenberg, H. BIOCHEM. J., Vol 51, 1952, pp 606-610.

12. Barker, S. A., and Summerson, W. H. J. BIOL. CHEM., Vol 138, 1941, pp 535-537.

13. Galaktionova, G. V., and Strzhizhovskiy, A. D. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1973, pp 49-51.

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EFFECT OF RHEOPOLYGLUCIN ON BLOOD CLOTTING FACTORS OF THE AORTA, MYOCARDIUM AND VENAE CAVAE DURING HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 74-76

[Article by V. I. Inchina, submitted 1 Feb 78]

[Text] Thromboembolisms and hemorrhages are found quite often in patients who have been on prolonged bed rest, as well as in hypokinetic animals [1-6]. However, the pathogenesis of blood clotting changes associated with restricted movement has not yet been sufficiently investigated, and in particular there is no information about the state of the tissular system of hemostasis. Yet, it was established in recent years that the vascular wall and myocardium play an important role in regulating the process of blood clotting and fibrinolysis [7, 8]. It was also found that it is possible to correct pharmacologically disturbances in the tissular system of hemostasis [9, 10]. In the opinion of some authors, hypokinesia is one of the factors involved in development of atherosclerosis [11-14]. For this reason, it is interesting to investigate the blood clotting and fibrinolytic properties of vessels and the myocardium under hypokinetic conditions. In view of the high efficacy of low molecular dextrans in the treatment of thromboembolic complications, we tried to determine their influence on the tissular system of hemostasis.

Methods

The studies were conducted on 43 chinchilla rabbits weighing 2-3 kg. Their movements were restricted by the method of V. V. Tyavokin [14]. The first group of animals (12 rabbits) were kept in special cages for 14 days; the second group (12 rabbits) was given rheopolyglucin injections (10 mℓ/kg weight) in the lateral vein of the ear during the same period of hypokinesia. Upon completion of the experiment, the animals were sacrificed, and extracts in a concentration of 1:100 were prepared from the myocardium, aorta (layered) and venae cavae. In addition, we examined the vessels and myocardium of 19 rabbits maintained under ordinary conditions. We tested blood clotting and fibrinolytic properties of the extracts using conventional methods [15].

We used the euglobulin method, as modified by V. P. Skipetrov [16], to test fibrinolytic properties of tissues. This technique permits demonstration of inhibitors of fibrinolysis and their interaction with activators of this process. For this purpose, we conducted two series of in vitro experiments: In the first series, we added 0.5 mℓ extract to the reacting system (8 mℓ distilled water + 0.15 mℓ 1% acetic acid + 0.5 mℓ donor plasma), and placed it in the refrigerator for 45 min. Acetic acid precipitates activators of fibrinolysis, while inhibitors remain in the supernatant. In the second series of experiments, after incubation of the mixture, we added 0.5 mℓ extract directly to the euglobulin fraction of plasma. In this case, both activators and inhibitors of fibrinolysis were present in the test tube. The obtained results were submitted to processing by the method of variation statistics using a Nairi-2 computer.

Results and Discussion

There was no change in overall thromboplastic activity of vessels and the myocardium under hypokinetic conditions, and it increased by about 5 times with administration of rheopolyglucin. After 2 weeks of hypokinesia, the extracts of intima, myocardium and venae cavae increased plasma heparin tolerance less than in intact animals. After administration of dextran, extracts of the intima, adventitia and venae cavae increased plasma tolerance to heparin more intensively. Administration of rheopolyglucin prevented the decrease in antiheparin activity of the aorta and venae cavae. At the same time, dextran enhanced the anticoagulant properties of the intima (by 9.1%) and attenuated the influence of the media, adventitia and myocardium on the second stage of coagulation. There was normalization of activity of prothrombin complex enzymes in the wall of the venae cavae. Extracts of the intima prolonged plasma prothrombin time without factor V (by 12.8%), whereas the aortic intima of rabbits did not affect this parameter after hypokinesia.

Hypokinesia caused an increase in antithrombin content of the aorta and myocardium and diminished it somewhat in veins. Rheopolyglucin prevented depletion of anticoagulant resources of veins, and did not affect anticoagulant activity of the aorta. In the myocardium, the antithrombin level dropped to base values.

There was significant enhancement of fibrin-stabilizing properties of vessels and the myocardium during hypokinesia. The fibrinase level of the intima rose by almost 3 times and that of the media by 5 times. Prolonged administration of rheopolyglucin diminished the activity of the fibrin-stabilizing factor in virtually all of the tissues examined.

Hypokinesia caused an increase in activators of fibrinolysis in vessels and the myocardium; however, the overall fibrinolytic capacity of tissues remained low due to a significant amount of plasminogen inhibitors. Administration of rheopolyglucin did not alter the amount of activators of the enzymatic process, but appreciably lowered the level of inhibitors, which increased significantly the fibrinolytic potential of the vascular wall and myocardium.

It was established that restricted movement elicits significant changes in the terminal branch of the vascular system. Thus, constriction of the arteriolar lumen, dilatation of venules, appearance of recessed sacculations and increased capillary permeability were demonstrated in the myocardium of hypokinetic rabbits [6, 17]. Such changes in the vascular wall, combined with the demonstrated changes in the tissular system of hemostasis, lead to impairment of microcirculatory hemostasis. In recent times, low molecular dextrans have found broad applications in the treatment and prevention of thromboembolic complications. The capacity to lower functional activity of formed blood elements is one of the factors involved in the high efficacy of these products [18-20]. It was established that low molecular dextrans affect mainly processes of thrombinogenesis and fibrinogenesis; they impair clot retraction and increase fibrinolytic activity of blood [21-23]. Impairment of longitudinal and transverse polymerization of fibrin monomers is probably the cause of formation of a friable, poorly retractable clot [8, 24, 25]. As we know, tissular fibrinase, decreased activity of which was found on the 14th day of hypokinesia with administration of dextran, plays an important role in the process of conversion if fibrin S into fibrin I (insoluble fibrin). Rheopolyglucin, which normalizes the rheological properties of blood and diminishes aggregation of formed elements, improves microcirculation. However, complete restoration of circulation can occur only when capillaries are free of fibrin. Evidently, by lowering the activity of inhibitors of fibrinolysis in the vascular wall and myocardium, rheopolyglucin enhances the effect of plasminogen activators, accelerating lysis of the friable clot. This process is the most intensive in veins. The increase in fibrinolytic potential of the aorta, myocardium and venae cavae under the influence of rheopolyglucin causes rapid removal of fibrin clots from capillaries and restoration of impaired circulation.

BIBLIOGRAPHY

1. Filatova, L. M., and Anashkin, O. D. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 6, 1968, pp 36-39.

2. Parin, V. V.; Krupina, T. N.; Mikhaylovskiy, T. P.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1970, pp 59-64.

3. Anashkin, O. D.; Zheltova, O. P.; and Kazanskaya, G. A. Ibid, No 2, 1972, pp 169-170.

4. Kudryashov, B. A.; Lamovskaya, E. G.; Shapiro, F. B.; et al. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 7, 1973, pp 1108-1113.

5. Filatova, L. M. in "Sistema svertyvaniya krovi i fibrinoliz" [The Blood Clotting System and Fibrinolysis," Saratov, 1975, pp 472-473.

6. Aleksina, L. A. in "Vsesoyuznyy s"yezd anatomov, gistologov i embriologov. 8-y. Tezisy" [Summaries of Papers Delivered at 8th All-Union Congress of Anatomists, Histologists and Embryologists], Tashkent, 1974, p 14.

7. Kuznik, B. I., and Skipetrov, V. P. "Formed Blood Elements, the Vascular Wall, Hemostasis and Thrombosis," Moscow, 1974.

8. Rabi, K. "Localized and Diffuse Intravascular Coagulation," Moscow, 1974.

9. Sopina, N. V.; Petrus', V. G.; and Kovalenko, A. N. in "Geparin. Fiziologiya, biokhimiya, farmakologiya i klinicheskoye primeneniye" [Heparin: Physiology, Biochemistry, Pharmacology and Clinical Applications], Moscow, 1973, pp 286-288.

10. Bogomolova, Ye. K. "Protective Anticoagulant Reactions in the Case of Intravascular Blood Clotting and Stimulation Thereof With Vasoactive Products," author abstract of doctoral dissertation, Perm', 1975.

11. Sokolov, N. Ye. ARKH. ANAT. [Archives of Anatomy], No 4, 1972, pp 48-52.

12. Mihaylova, O. M. in "Voprosy funktsional'noy anatomii sosudistoy sistemy" [Problems of Functional Anatomy of the Vascular System], Moscow, 1973, pp 124-125.

13. Karupu, V. Ya., and Ferents, A. I. in "Meditsinskiye problemy fizicheskoy kul'tury" [Medical Problems of Physical Culture], Kiev, Vyp 4, 1974, pp 78-83.

14. Tyavokin, V. V. "Hypodynamia and Cardiovascular Pathology," Saransk, 1975.

15. Baluda, V. P.; Malyarovskiy, V. N.; and Oyvin, I. A. "Laboratory Techniques for Examining The Blood Clotting System," Moscow, 1962.

16. Skipetrov, V. P. LABOR. DELO [Laboratory Record], No 8, 1969, pp 482-484.

17. Savik, Z. F., and Cherkay, A. D. BYULL. EKSPER. BIOL., No 9, 1974, pp 119-121.

18. Ricketts, C. R. BRIT. MED. J., Vol 2, 1966, pp 1423-1426.

19. Lareng, L.; Ducos, J.; Boisson, L.; et al. PRESSE MED., Vol 75, 1967, pp 341-344.

20. Larcan, A.; Stoltz, J. F.; and Alexandre, P. PATH. ET BIOL., Vol 17, 1969, pp 729-732.

21. Savel'yev, V. S.; Dumpe, E. P.; Shestakov, V. A.; et al. PROBL. GEMATOL. [Problems of Hematology], No 4, 1974, pp 7-13.

22. Rakhmayeva, V. A.; Guseynov, Ch. S.; Belorusov, O. S.; et al. in "S"yezd khirurgov Rossiyskoy Federatsii. 4-y. Trudy" [Proceedings of 4th Congress of Surgeons of the Russian Federation], Perm', 1975, pp 360-361.

23. Shestakov, V. A.; Il'in, V. N.; Aleksandrova, N. P.; et al. KARDIOLOGIYA [Cardiology], No 11, 1976, pp 87-92.

24. Dugdale, M.; Novzinger, J. D.; and Murphey, F. THROMBOS. DIATHES. HAEMORRH. (Stuttgart), Vol 15, 1966, pp 118-130.

25. Raby, C., and Vairel, E. GAZ. MED. FR., Vol 74, 1967, pp 4829-4845.

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EFFECTS OF ACCELERATIONS ON THE EARLY STAGE OF RADIATION LESION IN ANIMALS

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No 6, 1979 pp 76-77

[Article by V. V. Antipov, D. N. Gavrilyuk, B. L. Razgovorov and
B. I. Davydov, submitted 1 Feb 79]

[Text] We know that accelerations can have a substantial effect on the course and outcome of radiation lesions [1-2]. Analysis of studies dealing with the combined effect of accelerations and ionizing radiation shows that the modifying influence of the dynamic factor on the body's reaction to radiation depends on the order and intensity of exposure to them, intervals between them, etc. Accelerations may either attenuate or enhance the reaction to radiation. We submit here data on the influence of accelerations on the course of the primary reaction. This question had not been reflected in the literature previously.

Methods

We conducted experiments on 136 rats and 30 dogs. The animals were exposed to γ-radiation in a dosage of 800 R, delivered at a dose rate of 5-28 R/min with lead shielding [3] of the middle third of the abdomen. Under the shield, the radiation dose constituted 80 R for rats and 160 R for dogs. Survival constituted 75±6% for protected rats and 100% for protected dogs.

Transverse ($+G_x$) accelerations were generated on a centrifuge with a 4.2 m arm. Rats were immobilized by the limbs and head, and dogs only by the limbs. Rats were submitted to accelerations of 30 units lasting 2 min, and dogs were exposed to 8 units for 3 min. The gradient of acceleration build-up constituted 1 and 0.27 units/s, respectively.

There were 15-20-min intervals between exposures. During the period of the primary reaction of dogs, we studied their general condition, reaction to feed and vomiting reaction (number of times they vomited, time of onset and termination) over a period of 8-24 h.

The rats did not vomit. However, x-ray examination of function of the gastro-intestinal tract (GIT) revealed that the severity and duration of functional disturbances in irradiated rats were related to the radiation dose [4]. This enabled us to use GIT functional disturbances in irradiated rats as an approximate model of the primary reaction. We evaluated the initial stage of radiation sickness in rats on the basis of change in evacuatory function of the stomach 20 min and 2 h after the last exposure.

The experimental data were processed, with calculation of arithmetic mean (M) or median (Me), as well as mean error (m) and confidence intervals according to Student or Fisher.

Results and Discussion

Table 1 lists the results of the experiments on rats. In control animals (first group), there was uniform emptying of the stomach within 1-4 h, and GIT tonus was normal. Accelerations (2d group) led to some retention ($P>0.05$) of evacuation of the stomach. This was not associated with impairment of its tonus. Atonia was observed in the intestine.

Table 1. Effect of the combination of radiation and $+G_x$ accelerations on time of emptying of the stomach of rats with shielded abdomen

Animal group	Experimental conditions	Time after exposure	
		20 min	2 h
1	Control	2.4±0.4 (15)	2,8±0.6 (15)
2	Accelerations	3.2±0.8 (12)	3,6±1.0 (12)
3	Radiation	26±3 (18)	18±3 (16)
4	Radiat. + acceler.	18±7 (12)	17±6 (12)
5	Acceler. + radiat.	13±3* (12)	14±6 (12)

*$P<0.05$, as compared to the 3d group.

Note: The number of animals is given in parentheses.

In irradiated animals (3d group) there was 6-11-fold retention of evacuation due to pylorospasm and change in tonus of the stomach. There was prevalence of signs of dystonia and dyskinesia in the intestine.

Accelerations did not induce reliable changes in peristaltic and evacuatory function and tonus of the stomach of animals whose abdomen was shielded during irradiation (4th group).

When accelerations preceded radiation (5th group), there was a reliable, brief attenuation of functional disturbances of the GIT induced by radiation at the early stages; no modifying effect was demonstrable after 2 h.

Exposure of dogs to radiation in a dosage of 800 R with shielding of the abdomen induced vomiting an average of 2 times (Table 2). The vomiting reaction stopped 1 h after irradiation. At the same time, manifestation of some of the other symptoms of the primary reaction, such as general and alimentary depression, lasted an average of 3.5 h in the same dogs.

Table 2. Manifestation of primary reaction in dogs exposed to radiation with shielding of the abdomen and accelerations (n = 10)

Group	Experimental conditions	Vomiting					Alimentary and gen. depression		
		number of dogs	%	frequency of vomit. (Me)	duration of vomit.		number of dogs	%	duration (Me), h
					start (Me)	end (Me)			
1	Radiation	6	60 (26—83)	2 —	35 —	60 —	6	60 (26—83)	3,5 —
2	Rad.+accelerations	5	50 (19—81)	4 —	25 —	105 —	9	90 (56—100)	5 —
3	Acceler. + radiat.	6	60 (26—83)	2 —	12 —	62 —	6	60 (26—83)	2,5 —

Note: The confidence interval for P = 0.05 is given in parentheses.

Exposure of irradiated dogs to accelerations aggravated the manifestations of the primary reaction: more frequent and longer lasting vomiting, as well as longer duration (up to 5 h) of general and alimentary depression.

Exposure to accelerations prior to radiation did not have an appreciable effect on the tested parameters of early radiation vomiting. However, the symptoms of alimentary and general depression were present for a somewhat shorter time (up to 2.5 h).

Thus, a comparison of the results of experiments on rats and dogs shows that exposure to accelerations prior to radiation attenuates the primary reaction of both rats and dogs. Exposure to accelerations of irradiated animals induced effects in different directions: attenuation of GIT disturbances at the early stage of radiation lesion in rats, and intensification of some manifestations of the primary reaction in dogs.

The mechanism of the modyifying effect of preradiation accelerations on the primary reaction has not been sufficiently studied; special investigations will be required to comprehend it.

Thus, accelerations may have an modifying effect on manifestation of the primary reaction to radiation.

BIBLIOGRAPHY

1. Antipov, V. V.; Davydov, B. I.; Verigo, V. V.; et al. in "Osnovy kosmicheskoy biologii i meditsiny" [Fundamentals of Space Biology and Medicine], Moscow, Vol 2, Bk 2, 1975, pp 243-267.

2. "Central Nervous System Functions Under the Combined Effect of Stress Factors (Ionizing Radiation, Accelerations and Vibration)," Moscow, 1973.

3. Razgovorov, B. L.; Morozov, V. S.; Shashkov, V. S.; et al. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 4, 1965, pp 411-429.

4. Gavrilyuk, D. N., and Krasnykh, I. G. RADIOBIOLOGIYA [Radiobiology], No 1, 1977, pp 122-125.

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TEST IRRADIATION OF CHRONICALLY IRRADIATED DOGS FOR EVALUATION OF HEMOPOIETIC SYSTEM FUNCTION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 78-80

[Article by T. Ye. Burkovskaya and B. A. Markelov, submitted 15 Nov 77]

[Text] Protracted exposure to radiation leads to attenuation of radiation lesion, and sometimes the hematological status of dogs presents no obvious disturbances, in spite of accretion of rather high doses of radiation [1, 2 and others]. In order to determine the severity of lesion and state of compensatory mechanisms of the hemopoietic system, it is expedient to use functional loads [3, 4]. In this study, we used acute irradiation as such a load [5, 6].

Methods

This study was conducted on male mongrel dogs kept in a ^{60}Co gamma field for 6 years.* The dose rate of chronic radiation constituted 0.17 rad/day. Against the background of chronic irradiation, the dogs were exposed to acute radiation 3 times a year, in doses of 8, 8 and 42 rad (1st group), 42, 42 and 42 rad (2d group). One group of animals was maintained under the same conditions for 6 years, with the exception of the radiation factor (3d group--biological control). The Table indicates the experimental set-up and cumulative doses. Six years after the start of the experiment, we used acute radiation in a dosage of 125 rad (dose rate 10 rad/min). This dosage induces a rather distinct reaction in healthy dogs, with reference to blood, the parameters of which revert to normal within 30-40 days [7].

We examined peripheral blood and bone marrow. In comparing the experimental groups, we used the T criterion of Student, U criterion of Wilcoxson-Mann-Whitney and Q criterion of Rosenbaum [8].

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*Comprehensive substantiation, structure of the experiment and irradiation techniques were furnished in [5 and 6].

Results and Discussion

Moderate decrease in myeloid hemopoiesis and distinct activation of erythroid hemopoiesis were observed in dogs exposed to radiation for 6 years [9, 10]. The erythroblast element of bone marrow exceeded the tope range of the physiological norm. Depression of leukoblast hemopoiesis was manifested by a decrease in number of leukocytes in peripheral blood, mainly referable to granulocytes, and decrease in leukoblast element of bone marrow. The changes were the most marked in the 2d year of the experiment. Some improvement was observed for the next 2 years, and in the 5th and 6th years there was stabilization of bone marrow disturbances and some normalization of leukocyte composition if blood with reliably ($P<0.01$) increased erythrocyte content of peripheral blood. No disturbances were demonstrable in the system of thrombocytopoiesis.

Experimental set-up and cumulative doses

Group	Number of dogs	Median tissue doses, rad/year			Cumulative dose in 6 years, rad	Number of dogs submitted to test radiation in a dose of 125 rad
		chronic irrad.	repeated irradiation	total		
1	12	62	42+8+8	120	720	6
2	10	62	42+42+42	188	1130	4
3 Control	12	0	0	0	0	6

There were distinct differences between the groups of healthy and preirradiated animals with respect to severity of the reaction to acute radiation in a dosage of 125 rad. They were already manifest at the stage of the primary reaction, which was characterized by initial neutrophilia. The most marked neutrophil reaction was observed in dogs that were not submitted to preirradiation (Figure 1). Neutrophilia occurred at the same time in dogs preexposed to radiation in a cumulative dose of 720 rad, but it was reliably less marked ($P = 0.01$, according to the U criterion). In dogs that received a cumulative dose of 1130 rad prior to test irradiation, there was either no neutrophil reaction, or else it was insignificant and presented a maximum at an earlier time.

There was a decrease in lymphocyte content of blood at the stage of the primary reaction (see Figure 1). This decline was less marked ($P<0.01$) in dogs preexposed to a higher dose of radiation (2d group).

The difference between group indices was also manifested in the stages of the primary and secondary depletion. In irradiated dogs, the decrease in neutrophil and leukocyte content occurred sooner, regardless of dosage of prior radiation (Figure 2, A and B). Neutropenia and leukopenia were more severe and lasted longer in animals submitted to the maximum dose of pre-radiation. The parameters began to recover after 42 days, and restoration was less complete (to 65% by the 150th day). According to the dynamics of these parameters, the changes were reliable (P<0.01).

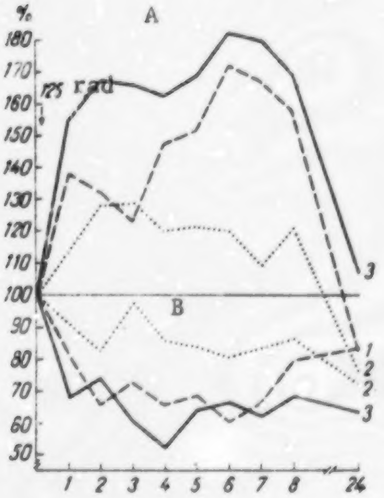

Figure 1.
Primary reaction of dogs to acute radiation in a dose of 125 rad. X-axis, hours after test radiation; y-axis, percent of initial value.

A) neutrophils
B) lymphocytes
Here and in Figures 2 and 3:
1) first group
2) second group
3) control

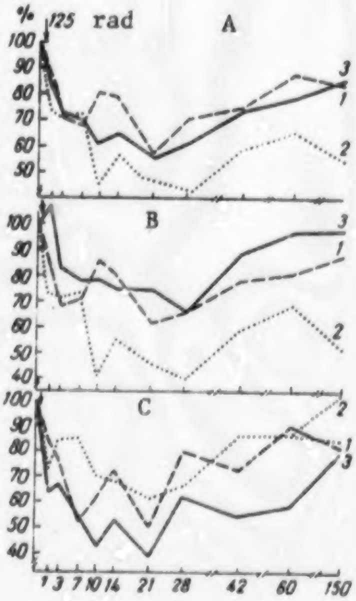

Figure 2.
Leukocyte composition of blood after test irradiation

A) leukocytes
B) neutrophils
C) lymphocytes
Here and in Figure 3:
X-axis, days after exposure;
y-axis, percent of base value

The absence or mildness of primary neutrophilia, as well as the distinctions referable to the course of the stages of depletion and restoration in pre-irradiated animals, are apparently attributable to the shortage of granulocytes in the bone marrow pool of maturation and storage, which is the main supplier of granulocytes to blood, particularly during the period of the primary reaction and the first 3 days after acute irradiation. The reduction of the bone marrow granulocyte reserve was demonstrated in dogs by means of the pyrogenal test in the 5th year of chronic irradiation [11]. In addition, acute irradiation against the background of diminished granlocytopoiesis, which resulted from the long-term effect of chronic radiation, apparently also led to disturbances in the system of granulocyte replacement, including the pool of stem cells and, as a consequence, more prolonged neutropenia.

In preirradiated dogs, the number of lymphocytes changed to a lesser extent at the depletion phase, as it did at the primary reaction phase, than in control animals (Figure 2C). The difference between the 2d and 3d (control) groups was statistically reliable (P = 0.01).

The changes in erythrocyte and reticulocyte content were similar and insignificant in all groups (Figure 3, A and B). The absence of differences referable to erythrocytes, between healthy and preirradiated animals, was indicative of preservation of a high capacity for repair and high activity of compensatory mechanisms of this system, unlike the myeloid system, in irradiated dogs.

After test irradiation, the thrombocyte content of peripheral blood dropped unreliably by a mean of 50% in all groups of dogs (Figure 3C).

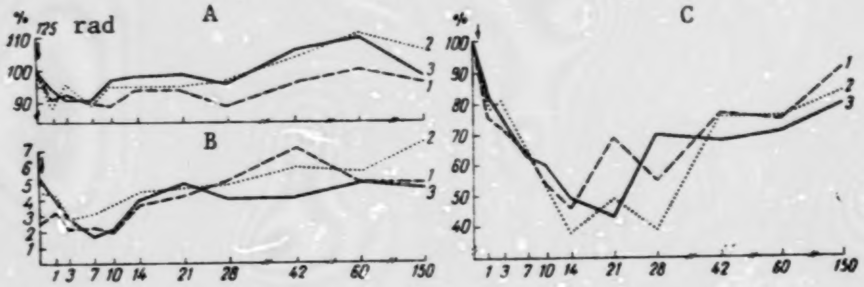

Figure 3. Change in number of erythrocytes (A), reticulocytes (B) and thrombocytes (C) after delivery of test radiation in a dose of 125 rad

As can be seen from the submitted data, there were abortive increases in number of cells in the dynamics of cells referable to different directions of differentiation (neutrophils, lymphocytes, erythrocytes and thrombocytes) (see Figures 2 and 3). The abortive rise is apparently related to some restoration of migration of stem cells from the pool, and this at the level of a single uncommitted precursor.

Examination of bone marrow punctates revealed that no significant differences existed between groups with regard to the parameter of overall cellularity and cytological composition of all blast elements of the bone marrow.

Thus, by using acute radiation in a dose of 125 rad, we were able to demonstrate functional deficiency of myeloid hemopoiesis in dogs submitted to long-term chronic radiation; this deficiency was not demonstrable in ordinary morphological examinations of blood and bone marrow. The obtained results are indicative of a reduction in the bone marrow reserve of mature granulocytes, and this is more marked in dogs preirradiated in a dose of 1130 rad, as well as disturbances in the system of postradiation renewal of granulocytes. Repair and compensatory-adaptive capabilities remain at a rather high level in the erythroid system.

BIBLIOGRAPHY

1. Akoyev, I. G. "Problems of Postradiation Recovery," Moscow, 1970.

2. Spalding, J. F.; Holland, L. M.; Prine, J. R.; et al. RADIAT. RES., Vol 55, 1973, p 453.

3. Bogatov, L. V. "Investigation of Functional State of the Blood System at the Long Term After Chronic Exposure to Gamma [illegible]ation," candidatorial dissertation, Moscow, 1965.

4. Gus'kova, A. K., and Baysogolov, G. D. "Radiation Sickness in Man," essays, Moscow, 1971.

5. Markelov, B. A. in "Somaticheskiye effekty khronicheskogo oblucheniya" [Somatic Effects of Chronic Irradiation], Moscow, 1972.

6. Popov, V. I.; Shafirkin, A. V.; and Yurgov, V. V. Ibid, p 17.

7. Cronkite, E. P., and Brecher, G. ANN. N.Y. ACAD. SCI., Vol 59, 1955, p 815.

8. Gubler, Ye. V., and Genkin, A. A. "Use of Criteria of Nonparametric Statistics for Evaluation of Differences Between Two Groups of Cases in Biomedical Research," Moscow, 1969.

9. Burkovskaya, T. Ye. KOSMICHESKAYA BIOL. [Space Biology], No 1, 1977, p 68.

10. Tsessarskaya, T. P.; Burkovsksya, T. Ye.; Zubenkova, E. S.; et al. in "Somaticheskiye effekty khronicheskogo oblucheniya," Moscow, 1972, p 35.

11. Zubenkova, E. S. Ibid, p 43.

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INSOLUBLE COLLAGEN CONTENT OF DOG TISSUES AFTER EXPOSURE TO LOW DOSES OF CHRONIC GAMMA RADIATION

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[Article by Z. A. Vinogradova, submitted 22 Mar 78]

[Text] We did not find any data in the literature concerning the effect of chronic irradiation on metabolism of collagen proteins. For this reason, our objective here was to study the insoluble collagen content of animal tissues at different stages of a chronic experiment. The conditions thereof were described in detail in the works of Yu. G. Grigor'yev et al.

Methods

We used 44 mongrel dogs, ranging in age from 1 to 3 years, 20 of which were exposed to radiation and 24 constituted the control. The first group was exposed to chronic ^{60}Co gamma radiation at the rate of 0.34 rad/day; the second group was exposed additionally to acute radiation in doses of 42, 8 and 8 rad at 4-month intervals, against the background of chronic exposure at the rate of 0.17 rad/day. The cumulative tissue doses constituted means of 245, 370, 495, 618 and 735 rad after 2, 3, 4, 5 and 6 years, respectively, of irradiation.

We assayed insoluble collagen content in experimental dogs (two animals were sacrificed from each group) by the hydroxyproline method of Neuman and Logan.

Results and Discussion

There were no reliable differences between the first and second groups of animals exposed to radiation for 6 years (to cumulative doses of 750 and 720 rad, respectively), with respect to insoluble collagen content (Table 1). This enabled us to combine the results for these groups in order to increase reliability.

There was a decrease in insoluble collagen content of organs and tissues (lungs, aorta, liver, tendon, cartilage and skin) of irradiated dogs as the accreted dosage increased (Table 2).

Table 1. Comparative data on insoluble collage content (mg% for dry tissue mass) in dogs of the first (750 rad) and second (720 rad) groups (M±m)

Tissue or organ	Group	
	1	2
Lungs	3,84±0,42	3,63±0,09
Aorta	4,96±0,63	5,37±0,69
Liver	3,90±0,34	3,27±0,26
Achilles tendon	3,57±0,45	3,52±0,31
Cartilage	6,39±0,66	5,36±0,72
Skin	4,51±0,49	4,78±0,79

Table 2. Insoluble collagen content (mg% for dry tissue mass) in dogs following chronic exposure to radiation (M±m)

Tissue or organ	Year of irradiation				
	2		3		4
	245 rad	control	370 rad	control	495 rad
Lungs	4,15±0,25*	10,6±0,63	3,07±0,24*	6,15±0.37	3,80±0,23*
Aorta	7,02±0,51	6,60±0,37	6,25±0,46	6.13±0.35	5,45±0.39
Liver	4,70±0,23	4,55±0.40	4.20±0,20	4.30±0.37	3.75±0,18
Achilles tendon	9,70±0,57*	7,30±0,57	4,40±0,26*	6,90±0,54	4,05±0,24*
Cartilage	8,67±0,78*	5,05±0,42	7,60±0,64*	5.27±0,44	6,50±0,59
Skin	5,90±0.52*	6,05±0,35	5,35±0,47	5,80±0,33	4,85±0,44

Tissue or organ	Year of irradiation				
	4	5		6	
	control	618 rad	control	735 rad	control
Lungs	5,30±0,32	3,60±0,22*	4,95±0,30	3,45±0.21*	4,60±0.26
Aorta	5,60±0,31	4,65±0,34	5.10±0,28	3,85±0.28	4,62±0.26
Liver	4,00±0,34	3,30±0,16	3,75±0,32	2,85±0.14*	3,50±0.30
Achilles tendon	6,52±0,51	3,72±0,22*	6,10±0,48	3,35±0.20*	5,70±0.45
Cartilage	5,50±0,46	5,37±0,48	5,70±0,47	4,25±0.38	5,92±0.49
Skin	5,55±0,32	4,32±0,39	5,30±0,30	3,80±0.34*	5,05±0,29

* $P<0,05$

The earliest changes were noted in lung tissue. Collagen content of lung tissue constituted one-fifth the control level in the 2d year of irradiation with accumulation of 245 rad. At this same time, an increase in insoluble collagen was noted in the tendons, whereas after 3 years of irradiation there was, on the contrary, a decrease. The amount of this protein in cartilage was high up to the 5th year of irradiation. A decrease in insoluble collagen occurred in the aorta and liver after accretion of 495 rad, and in the skin after 245 rad.

Age-related changes were demonstrated with respect to collagen content of the tissues examined (see Table 2). Thus, insoluble collagen content dropped from 10.6 mg% (4 years) to 4.6 mg% (8 years) in the lungs and from 6.6 to 4.6 mg% in the aorta. The decrease in insoluble collagen with advancement of age (8-9 years) and accretion of radiation dose (to 735 rad) is probably related to intensification of sclerotic processes. During exposure to radiation, conditions develop that favor polymerization of young forms of collagen and formation of coarse, inert fibers, the number of which increases with increase in duration of exposure.

The decline in metabolic activity of collagen in dog tissues with increase in age is the result of increase in covalent intramolecular and intermolecular bonds in the structure of collagen.

OBITUARIES

UDC: 612:929 Khazen

IONUSON MENASHEVICH KHAZEN (1901-1979)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 pp 82-83

[Article by editorial board]

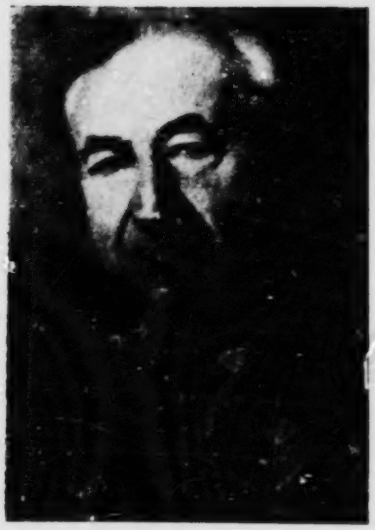
[Text] One of the prominent specialists in the field of aviation and space medicine, who made a substantial contribution to development of these disciplines, Prof Ionuson Menashevich Khazen, member of the CPSU since 1943, passed away on 20 June 1979, in his 79th year.

I. M. Khzen, a disciple of Academician I. P. Razenkov, reared in the traditions of the Russian phsyiological school of Academician I. P. Pavlov, was concerned with physiology of digestion, metabolism and nutrition in the 1930's, and from 1937 on he worked in the field of aviation medicine, studying digestive functions in an environment with low pressure and low oxygen content; he participated in the expeditions to Mount El'brus of the USSR Academy of Sciences in 1939-1940.

The works of I. M. Khazen at the Institute of Nutrition (1930-1933) and Institute of Experimental Medicine (1934-1941) contain basic data about the mechanisms of neurohumoral regulation of digestive glands. They made it possible to delve into the essence of the mechanisms of regulation of digestion at high altitudes and to make a breakthrough in solving several practical problems of altitude physiology.

On the very first days of the war, I. M. Khazen joined the ranks of the Soviet Army and served as head of an evacuation point for 3 years, giving all his efforts to restoring the health of wounded soldiers and commanders. His homeland was very appreciative of his deeds during the years of the Great Patriotic War, and bestowed many orders and medals upon him.

In 1944, I. M. Khazen was assigned to the military faculty of the Central Institute for Advanced Training of Physicians and, together with Prof V. V. Strel'tsov, participated in organizing the chair of aviation medicine, where he worked for 17 years, starting as deputy head and then (from 1956 to 1961) as head of the chair.



In the years that I. M. Khazen worked on the chair and under his supervision, dozens of research projects were conducted in the field of altitude physiology, physiology of accelerations; the effects of many extreme factors (pressure changes, vibration, physical stress, etc.) were studied, more than 20 candidatorial and several doctoral dissertations were defended.

I. M. Khazen was engrossed with theoretical and applied problems of space physiology from 1961 on.

In 1964-1970, at the initiative of I. M. Khazen two "Guides on Space Biology and Medicine" and several collections of scientific articles were published, which he edited (in collaboration with other scientists). He was an active participant in the first All-Union conferences on aerospace biology and medicine. He was one of the initiators of the journal, KOSMICHESKAYA BIOLOGIYA I MEDITSINA [Space Biology and Medicine] and a member of its first editorial board. In all, I. M. Khazen published about 200 scientific works during the more than 50 years of his scientific endeavors, including the monograph, "Essays on Space Physiology" (1967) in collaboration with V. V. Parin, R. M. Bayevskiy and M. D. Yemel'yanov.

I. M. Khazen was very active in scientific and public work to make known the advances in Soviet science. For 25 years he was the chairman of the section for aviation and space medicine of the Moscow Physiological Society, a member of the board of the All-Union Physiological Society imeni I. P. Pavlov, and for many years he was a member of the organizing committee for Tsiolkovskiy Lectures and a member of the Scientific Council of the State Museum of the History of Cosmonautics imeni K. E. Tsiolkovskiy. The activities of I. M. Khazen directed toward dissemination of the ideas of K. E. Tsiolkovskiy and achievements of Soviet aerospace medicine were highly rated: he was the recipient of medals imeni K. E. Tsiolkovskiy, S. P. Korolev and Yu. A. Gagarin.

His purposefulness and high-mindedness in science, rich scientific erudition, selfless involvement in the life and endeavors of his colleagues, his great general sophistication and intelligence earned much respect for I. M. Khazen on the part of his disciples and followers, and inspired a sense of gratitude in all those who worked with him.

UDC: 613.693:929 Druzhinin

YURIY PAVLOVICH DRUZHININ

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 6, 1979 p 83

[Article by editorial board]

[Text] Yuriy Pavlovich Druzhinin passed away on 20 April 1979, in his 42d year, after a serious and brief illness. A scientist, whose name is linked with development of a number of problems of space biology, biorhythmology and heliobiology, passed away in his prime.

The biological effects of different components of cosmic radiation, the combined effect of cosmic radiation and other space flight factors, fluctuations in the course of 24 h of radiosensitivity of animals and man, individual distinctions of rhythms of physiological and biochemical processes, relationship between morbidity of the public and various manifestations of solar activity--this is far from a complete list of the topics that were the subjects of research for Yuiry Pavlovich and the team he headed.

The results of this research were published in more than 60 scientific works and summarized in the doctoral dissertation he prepared.

Yuriy Pavlovich expounded an original hypothesis concerning the link between the magnitude of the modifying effects of nonradiation environmental factors on radiation effects and the circadian rhythms of radiosensitivity; he defined the range of the coefficient of the modifying effect of weightlessness; he plotted the routes toward demonstration of the distinctions of the body's reaction to deleterious factors based on the distinctions of circadian rhythm of vital processes; he obtained data indicative of appreciable elimination [leveling off] of the influence of heliogeophysical factors on functional manifestations and viability of sick and healthy people in a large modern city; he accomplished an enormous amount of work dealing with development of a modern stand base for biorhythmological magnetobiological and heliobiological research.

Yuriy Pavlovich stood out because of his uncommon organizational skills, high-mindedness and high sense of responsibility for work entrusted to him, his kindness toward people, joie de vivre and enthusiasm. He was greatly respected and loved by his friends and fellow workers.

The bright memory of Yuriy Pavlovich Druzhinin, an exceptionally sensitive and sincere man, will remain forever in the hearts of all who knew him.

UDC: 612.17+616.12]:929 Fogel'son

LAZAR' IZRAILEVICH FOGEL'SON

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 6, 1979 p 83

[Article by editorial board]

[Text] Prof Lazar' Izrailevich Fogel'son, honored scientist of the RSFSR, died on 10 June 1979.

Three generations of physicians were educated by his comprehensive monographs: "Fundamentals of Clinical Electrocardiography" and "Diseases of the Heart and Vessels."

L. I. Fogel'son did some original work on physiology of the heart: the mechanism of influence of extracardiac nerves on the myocardium. He was the first to propose (1949) and successfully test a method of electric pulse therapy of auricular fibrillation, and it was gained wide recognition.

All those who knew L. I. Fogel'son, the outstanding scientist and cardiologist, personally and those who studied from his books will remember him kindly.

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SCHEDULING WORK AND REST PERIODS DURING LONG-TERM SPACE FLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1980 pp 3-8

[Article by B. S. Alyakrinskiy, submitted 7 Mar 78]

[English abstract from source]

Proper arrangement of work-rest cycles of crewmembers in long-duration space flight is a practically important task of space ergonomics, a field of science studying man's work capacity and methods of its increase. The basic principle of space ergonomics assuring high efficiency of space crewmembers is to cover every aspect of their activities. Of particular importance is the use of laws of biorhythmology, in order to select candidates least susceptible to desynchronosis and closely resembling each other in their biorhythmological status. At the present time, work—rest cycles in a prolonged space flight should be arranged on a 24-hour basis with a normal day—night alternation, including 8-hour night sleep and 2-hour day rest. Optimization of cosmonauts' activities in space demands that they strictly adhere to the recommended work — rest cycle; this can be achieved through their highly motivated desire only.

[Text] Elaboration of the principles involved in wise organization of labor and rest for representatives of any profession, including cosmonauts, is one of the tasks of ergonomics, a scientific direction that now deals with studies of work performance (for the purpose of improving its efficiency), mainly within "man--machine" systems. Searching for sources of increasing efficiency mainly or exclusively within the framework of an isolated work process is a typical feature in numerous ergonomic studies of West European and American researchers.

Montmollen, one of the leading West European specialists in the field of scientific organization of labor [efficiency experts], believes that ergonomics is the "technology of linkages in 'man--machine' systems," or "... more precisely, the technology of factors that characterize interaction between man and machines" [1, p 16]. True, Montmollen immediately adds that "ergonomics can be defined as the study of work performance for the purpose of improving it" (ibid, p 16), already broadening somewhat the tasks, with which this discipline deals. However, in spite of this stipulation, Montmollen, like many other specialists in organization of labor, avoids interpretation of ergonomics in his studies in this field as the technology of links between man and machines.

Consideration of ergonomics solely as the technology of relations between man and machines reflects a purely pragmatic and strictly utilitarian approach to the problem of improving efficiency in the field of computer production. Upon closer scrutiny, such an approach is found to be overtly unfounded for solving the problem of improving work performance, since the framework of technology of the links between man and machine does not permit (and, in essence, cannot permit) exploration of all the possibilities of improving the productivity of labor, all reserves of efficiency and all sources of growth of professional productivity. Many of these sources are beyond the links between man and machine, beyond the confines of man's "work place." Indeed, is it not true that two employees, identical in qualifications, working under the same conditions, will not produce the same quantity or with the same quality because of differences in scheduling of their rest periods and differences in living conditions? And is it not true that the same individual does not change in his professional efficiency, depending on many factors that are far from professional ones (domestic, social and others)? And is it not apparent that not only an individual's professional reliability and efficiency, but his health, longevity (including occupational), level of physical and intellectual development, the entire system of his spiritual life depend largely, if not entirely, on the way he has organized his life, i.e., the actual work and rest regimen he has adopted?

If this is so, a genuinely scientific approach to the problem of high productivity of labor should take into consideration as many factors as possible (within the available range), which determine directly or indirectly the ongoing efficiency of man.

The principle of socialistic humanism, according to the very essence of which man's endeavors should not cause even the slightest detriment to his health or reduce to any extent the possibility of cultural and physical development, the possibility of active participation in the nation's sociopolitical life, is completely consistent with the requirement of a comprehensive approach to purely ergonomic problems. When put on such a basis, ergonomics concentrates on man, the real creator and maker, for whom work is the enjoyment of "play" of physical and intellectual capabilities. And only a science, the representatives of which study with equal thoroughness organization of both work itself and leisure, and time spent both at work and away from it, i.e., the entire order of life of an individual that does work that is needed by society, can cause labor to be transformed into a source of enjoyment of the play of physical and intellectual capabilities (and thereby increase its efficiency).

Thus, ergonomics as a scientific direction that combines the study of the correlation between efficiency of work and a man's life style, the entire order of his life and, in particular, the order of his professional activity (including factors characterizing interaction between man and machine), with the ultimate purpose of increasing the efficiency of labor, should include among its main tasks the development of the principles for wise organization of both work and leisure (including sleep). All of the foregoing also applies in full to the occupation of cosmonaut. Moreover, the occupation of a cosmonaut differs from most others primarily in that work and leisure, as well as the time spent on some sort of activity and time virtually free of such activity, can be only relatively, arbitrarily separated under the conditions of space flights. Cosmonauts who are aboard an orbital spacecraft, let alone an interplanetary one, are cut off from the contacts with people on earth, that are customary in form and scope, as well as from the entire surroundings of earth. Being dependent entirely on sturdiness of the craft, reliability of its numerous systems and, first of all, the life support system, even during periods of complete freedom from any duties they continue to perform the flight and to participate in fulfilling its general objective. Cosmonauts cannot "retreat to the rear from the front line of their mission," they cannot cut themselves off from the flight situation. Of course, even sleeping in space is not the same as sleeping on earth, since our emotional [spiritual] life never ceases enitrely during sleep and always bears the mark of events currently in progress. The links between the cosmonaut and the spacecraft are really vital, i.e., the welfare and life of the cosmonaut depend entirely on them and they cannot be severed at his will. The ties between the cosmonaut and a spacecraft are analogous to those of a pilot and his aircraft, and the vital need for the latter is also quite obvious. An experienced pilot, K. Katichev writes: "In the event of malfunction or difficult situation, any other piece of equipment, be it a motor vehicle, steam engine or ship, can be stopped, repaired, or else one can wait it out until the situation improves, and then continue on one's way, and this cannot be said about an aircraft. But whatever the problem with an aircraft and no matter how complicated the situation could become, a pilot cannot stop a flying aircraft and is compelled to find the correct solution making use of all his skill and ability" [2, p 24). The vital need for bonds between cosmonauts and a spacecraft is expressed in the special sensitivity of cosmonauts to various types of unexpected stimuli that are new to them. This is observed by the cosmonauts themselves: "In space," states pilot cosmonaut O. G. Makarov, "there is drastically heightened wariness...." [3]. Any danger signal, any new stimulus are perceived with equal acuity by all members of a spacecraft crew, whether or not they are busy with some sort of work or not. Aboard a spacecraft, not only the period of professional activity (shift of duty [watch]), but every moment of the cosmonauts' life, their entire life as a whole and its entire order are determined by the process of flying, they are "woven into its fabric." And for expressly this reason, assurance of a successful space mission is, in essence, an ergonomic task, this is achieved not only by means of scientific organization of work (professional activity) of cosmonauts, but scientific organization of their entire schedule in each 24-hour cycle. Hence, it is obvious that a thorough analysis must be made of this cycle in the ergonomic aspect.

The daily cycle is not simply the structure of periods of work, leisure and sleep in accordance with the natural alternation of night and day, adjusted to this alternation in accordance with considerations of convenience, economy, occupational or some other need. The daily cycle of our life is the genetically programmed rhythm of all body functions and processes; it is the rhythm of all of the body's vital systems that is endogenous in origin. Special studies, which have been conducted mainly by specialists in biorhythmology (chronobiology, in the terminology of American authors), a science dealing with biological rhythms, have shown that any organism that is complex to some extent is a very complicated oscillatory system, a distinctive array of numerous rhythms with the most diverse frequency, amplitude characteristics, positions of phase, range of straying [wandering], etc., and that in this array of rhythms the one with a frequency of about 24 h plays a particularly important role (hence its name, circadian, occurring approximately every 24 h).

The special role of circadian rhythms is attributable to the fact that they perform the function of a timing device (hence, their name of biological clock), that expressly they regulate the process of adaptation of the body to the environment in the form of its externally manifested activity (behavioral form of adaptation) and, consequently, they watch over the stability of an energy balance that is advantageous to the body, an expression of which is the relative stability of sleep and waking periods. For this reason, it is not surprising that there is a direct and close relationship between the welfare of the body and state of its circadian rhythms.

The state of biorhythmological welfare inherent in healthy man corresponds to relative stability of phase architectonics of its circadian rhythms. Impairment of these architectonics, i.e., phasic mismatching of circadian rhythms of different functions (desynchronosis), is associated with a decrease in efficiency, sleep disorders, impaired appetite, mood, digestion, appearance of neurological symptoms (severe irritability, pathological reflexes) and even organic diseases (gastritis, peptic ulcer and others). Desynchronosis occurs when changing time zones (transmeridional flights), when the customary schedule is altered, when there is unusual change in periods of light and darkness (Arctica, Antarctica), under the influence of various stress factors and with overfatigue. There is every reason to believe that there is a real danger of desynchronosis during space flights, whatever their mission.

In view of the biorhythmological data pertaining to the circadian rhythms of the body, it can be stated that successful organization of work and leisure in any area of endeavor is achieved only if such organization is based on the principle of rhythm, of a rhythm with very definite characteristics, first of all, with regard to frequency (duration of period) and position of the phase.

Application of the rhythm principle is the most important prerequisite for rational [wise] organization of man's life aboard a spacecraft. As a general postulate of space ergonomics, it can be maintained that any schedule for cosmonauts that is not governed by a rhythm is inacceptable to them.

However, subordination of the cosmonauts' life to a rhythm during flight is not the only prerequisite for rational organization of their work and leisure time. It is of exceptional importance for the pace of life aboard a spacecraft to be as close as possible to the customary rhythm on earth, i.e., a rhythm with a 24-hour period and constant position of the phase on a 24-hour scale. In this respect, the best variant of a space day would be a day that is identical to the day at the launching pad, provided that the cosmonauts had completely adjusted to the time zone at the spaceport. The problem of man's adjustment to a day that is not the same as on earth cannot yet be considered definitively solved. There are data to the effect that man can adjust to changes in length of a day (other than 24 h), but there are few such data, and they were obtained from studies conducted under different and, occasionally, radically different conditions. We cannot fail to concur with V. Bruce [4] that highly organized beings have difficulty adjusting to cycles, the period of which differs significantly from 24 h. This thesis of V. Bruce was confirmed in experiments on hamsters [4], in whom cycles with periods of 23.5, 24, 24.5 and 25 h (with equally long periods of light and darkness) altered the physiological sleep--waking rhythms, while cycles with periods of 22 and 23 h did not alter them. We studied adjustment of subjects (5 men in all) to 23- and 25-h days (1971-1972). Both the 23-h and 25-h cycles of sleep and waking state were not adopted by the subjects. In studies with shorter days, there was distinct manifestation of integrity of the 24-h periodicity of body temperature and excretion of potassium from the 7th-8th day on. It should be noted that the most marked signs of absence of adjustment to a 23-h day were demonstrable at the last stage of the experiment, when the difference between experimental and 24-h days diminished progressively, rather than at the time when it reached a maximum [12 h).

In the studies with a 25-h day, in addition to lack of adjustment to such a cycle, the subjects presented disturbances of phase architectonics of the circadian system. In the oldest subject (32 years of age), this was manifested by the finding that the lowest body temperature began to consistently shift from the start of the waking period to the end after the 5th day, while the maximum began to shift toward the start of the waking period, starting on the 7th day. As a result of such migration of phases of temperature rhythm, they shifted considerably in relation to the phases of the rhythm of potassium excretion, which is an indication of internal desynchronosis.

Use of a 24-h day aboard a spacecraft, which would be synchronous with the daily cycle at the spaceport, would mean that all crew members sleep at the same time. Scheduling of sleep should provide for at least 7 h duration. In any case (with the exception of emergencies and other extraordinary situations), the cosmonauts must adhere strictly to the sleep schedule, whether or not they want to sleep during the hours scheduled for it. Sleep should be viewed as a part of the flight program that is just as important as scientific experiments, observations, working with onboard systems, etc. Performing work during the time reserved for sleep should be categorically excluded. There is no need to specially discuss the importance of comfort of the place where the crew sleeps; it should be outfitted with due consideration of the factor of weightlessness and habits of each crew member.

The schedule for the day should provide, in addition to 7-8 h of sleep, mandatory rest for 2 h (during the waking peiord), organization of which is defined in advance (on the ground) by the individuals responsible for preparing the flight program (with the participation of specialists--physicians, psychologists, hygienists, etc.). The rest program should be prepared with mandatory consideration of the individuality of each participant in the flight, his desires in this respect, and it should be backed up by an adequate amount of appropriate material (books, film strips [or slides], tape recordings, table games and others).

A programmed schedule for the day (with due consideration of all the listed requirements) will reduce significantly the influence of the negative factors of long-term space flights on cosmonauts. However, this can be achieved only if the suggested schedule for work and rest is strictly kept. Punctuality in following the work and rest schedule can be achieved only if there is full awareness of the need and substantiation of such a requirement, a set on the vital importance of adhering meticulously to the program of the onboard day. Formation of such a set is not a single act, it is a lengthy and painstaking process. A set cannot be formed as a result of simple instruction, periodic reminders or a preliminary talk. It develops only if an individual not only is aware of the importance of adhering meticulously to the suggested work and rest schedule, not only understands the contents of this requirement, but is convinced of its vital importance. And conviction is usually formed in an individual over long segments of his life, as a result of intensive internal work which necessarily involves the intellect and emotions. Here, it is opportune to stress once more the advantage of the above-formulated general conception of ergonomics, within the framework of which studies are made not only of the "man--machine--object of labor--work environment" system, not only the links between components in this system, not only the work process per se, but the entire order of a man's life, everything that pertains to both work and free time. For expressly this reason, the problem of formation of the required sets, in particular, the set toward absolute adherence of cosmonauts to the prescribed work and rest schedule, which is based on the principles of scientific organization of man's life in space, is an ergonomic problem.

From this point of view, the problem of organizing the work place, recreation areas, places for sleeping and individual rest, as well as the problem of organizing joint work by crew members, minimizing the deleterious effects of the extreme flight conditions and, finally, the problem of using, if necessary, unusual daily sleep-waking rhythms aboard the spacecraft, are also ergonomic problems. The last mentioned problem merits special discussion.

At the present stage of development of cosmonautics, such distinctive flight elements as launching time, precession and deorbit shaping, landing time and any emergency situations could preclude (and in many cases have done so) scheduling the life of cosmonauts following the example on earth. True, at the present time, actually all the conditions to assure such scheduling, even for long flights, already exist, as indicated by the flights aboard Soyuz-26 and Soyuz-27 spacecraft, as well as Salyut-6 orbital space station. Elimination of the negative influence of disruptions in the daily cycle aboard a spacecraft (i.e., organizing the life of cosmonauts according to the ground-based schedule) does not, however, eliminate the danger of desynchronosis. As indicated by material in the literature and our findings, desynchronosis can occur (and does indeed occur) when man is exposed to the stress of the most diverse negative factors. We can include among such factors weightlessness as well (and, apparently, all of the other extreme factors of space flights). For this reason, it is of utmost importance to elaborate measures to reduce as much as possible the danger of desynchronosis, especially in the case of a lengthy flight. There are facts that indicate that resistance to the adverse effect of disruptions of the customary daily schedule is quite individual. "Substantial differences have been noted in the capacity to adjust to altered work--rest cycles: some subjects adjusted rapidly to unusual cycles, while others were either totally incapable of such adjustment or had great difficulty in adjusting" [5, p 165]. For expressly this reason, proper screening of candidates for long-term space flights is important.

American specialists recommend that crew members be compatible, with regard to circadian rhythms, in screening cosmonauts and manning crews [5]. This recommendation can be followed only if the flight program provides for simultaneous sleep of the cosmonauts, if conditions are provided for mutual induction that is instrumental in maintaining the same daily rhythm of life for all cosmonauts. But if the cosmonauts sleep at different times, their compatibility with regard to circadian rhythms would not be very important.

Biorhythmological screening of candidates for space flights should be performed as early as possible, the best time (if possible) being prior to their enlistment as cosmonauts. Properly gathered history, the results of routine observation by specialists (physicians, training supervisors), friends, relatives, etc., are very important. One must record the distinctions of sleep under any circumstances (how fast the candidate falls asleep and wakes up, whether sleep is continuous or intermittent, his capacity to fall asleep under unusual conditions, etc.).

This approach to training of spacecraft crews conforms entirely with the conception of space ergonomics, the area of competence of which extends to the entire order of cosmonauts' life. This conception also includes the requirement for "biorhythmological" arrangement of the interior of a spacecraft. If we agree that maintaining the circadian rhythm of man depends largely on strict organization of the system of time sensors, we should also agree that, in space, where there is always the danger of desynchronosis, "build-up" of time sensors, saturation of the internal environment of the spacecraft with these sensors, in particular, those that simulate not only the daily dynamics of light, temperature, humidity inherent in earth, but seasonal fluctuations of these factors, acquire special significance.

BIBLIOGRAPHY

1. Montmollen, M. "'Man--Machine' Systems," Moscow, 1973.

2. Katichev, K. VESTN. VOZDUSH. FLOTA [Vestnik of the Air Corps], No 9, 1955, pp 24-33.

3. Apenchenko, Yu. PRAVDA, 13 1 1975.

4. Bruce, V. in "The Biological Clock," Moscow, 1964, pp 60-90.

5. "Man Involved in Long-Term Spacecraft," Moscow, 1974.

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USE OF MATHEMATICAL METHODS FOR PREDICTING MAN'S CONDITION DURING SPACE FLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1980 pp 9-12

[Article by V. V. Verigo, submitted 28 Feb 78]

[English abstract from source]

Possibilities of applying mathematical methods and computers to solve problems of predicting the human health state in space flight are discussed. The use of methods of simulation modelling is recommended. Examples of their application are described.

[Text] The task of predicting man's healthy status and efficiency during space flights continues to be one of the most interesting and important tasks for modern space biology and medicine [1]. Previously obtained results [2, 3] warrant the belief that the need to develop mathematical methods of predicting dynamic processes in the human body would stimulate research of both applied and general biological importance. The development of reliable and comprehensive forecasting methods may also be useful to clinical medicine. It would be difficult to overestimate the importance of automated forecasting of man's condition and reliability as an element of an integral biotechnological complex when designing and predicting the development of new space equipment, including equipment for active control of healthy status and work fitness of cosmonauts. The objective of controlling man's health status under extreme conditions is in essence a question of situational control, the principles of which have been described [4, 5]. Situational control deals with the behavior and synthesis of organizing systems implemented by means of man-machine complexes. However, we shall not touch upon the problems of automated classification of a situation, decision making and correction of current and future condition of cosmonauts, and shall limit ourselves only to a discussion of questions of using mathematical methods and computers for evaluation and prediction purposes.

There are three routes for the use of mathematical methods and computers to forecast man's condition during space flights. The first is closely related to the most widely used method of expert forecasting. Here, intuition and experience of the team of experts play the leading role in forecasting, while the task for the mathematical service is merely to provide for optimum working conditions [mode]. The experts make use of both current information received in the course of a flight and data stored in banks, which contain information about prior flights and ground-based tests. The choice and formation of data arrays, use of statistical algorithms to compare and contrast them, as well as other necessary operations are performed by means of a system of interactive dialog.

The distinction of the variants of dialog systems that we are using and developing is that they allow an expert without special mathematical knowledge to work with data arrays and processing algorithms in an interactive mode on the basis of a rather low level computer language. On the other hand, there must be a possibility for on-line development of the set of procedures for processing data by specialist-mathematicians on the basis of developed algorithmic languages.

It was possible to meet both these requirements by breaking down the dialog system into two program components. One of them, the logic structure of which is made up of a combination of choice of data and choice of method of manipulating with them, provides for interaction between experts and the computer. The interactive dialog is conducted at will, through a display or printer, on a language that is as close as possible to a natural one. The other (monitor) program component makes it possible to conducted on-line adjustment of the program modulus and transcribe it into the library of absolute moduluses in the place of prior modification, after which it becomes accessible to the expert. There has been experience with the use of such a system for processing major complex, ground-based experiments. The choice of attributes of bases of data from natural and ground-based studies is made together with the experts.

Another direction in the use of mathematical methods is the use of an extensive group of forecasting algorithms, which are based on extrapolation of time series. With the use thereof, forecasts were made of pulse rate and respiration rate by means of nonlinear discrete filters and other methods. The results of using some of them were reported previously [6]. Figure 1 illustrates examples of forecasting the pulse rate of cosmonauts by means of regression equations, the coefficients of which were assessed dynamically using the method of stochastic approximation. The possibilities and range of application of this group of forecasting methods are not yet entirely apparent. In spite of the fact that satisfactory results are obtained in a number of cases, there is reason to believe that their potential is rather limited, if only because the mechanisms of adaptation and possible pathogenesis of physiological systems under new conditions are obviously not taken into consideration in the forecasting process. Nevertheless, we can hope that they will be a useful supplement to the traditional methods of medical experts, while some of them could be used for automatic analysis and forecasting of the condition of cosmonauts, particularly with the use of onboard equipment.

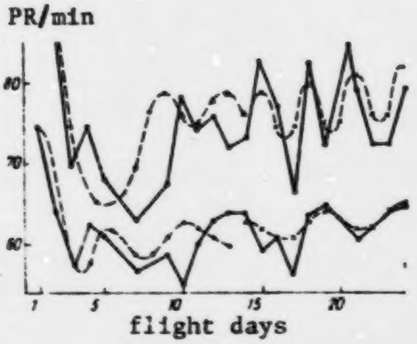


Figure 1.
Forecasting pulse rate (PR) of two crew members aboard Salyut-1 spacecraft. Solid line, actual values; dash line, forecast. The dots refer to the forecast after 6 days, triangles--after 12 days and x's after 14 days of flight

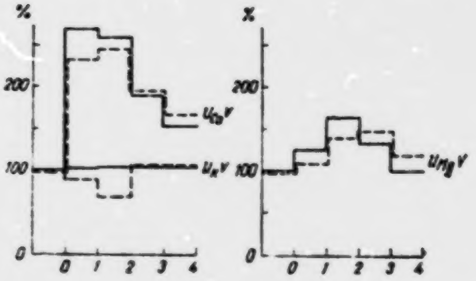


Figure 2.
Simulation of Ca, Mg and K excretion after hypertensive calcium load. Solid line, simulation; dash line, actual values.
X-axis, time (h); y-axis,
Y-axis, excretion (% of normal)

The third of the directions is simulation modeling. The theoretical bases of this method have been described previously [9]. Imitation modeling has been used with success in the national economy [7, 8]. The specifics of using a simulation model lies in multiple reproduction of a dynamic process. The process of setting conditions characterizing concrete realization thereof (initial conditions, exogenous factors, parameters of the model) is called setting a "scenario" in existing terminology. For simulation modeling in physiology, preparation of scenarios includes setting parameters determining the status or individual distinctions of the subject or specific physiological system, setting changes in time of exogenous conditions and, in the case of various hypotheses on physiological mechanisms, choice of hypothesis. This work is a creative process performed by an expert physiologist with the consultation and collaboration of a mathematician. At the present time, work is in progress to automate this procedure.

Current information and the results of prior studies are used in a dual manner in simulation modeling. In the first place, they are needed to formulate the assignment (scenario). In the second place, they can be used to identify unknown or approximately set parameters of models. For this purpose, a special module [block] was developed for identification of models of dynamic systems with a finite number of degrees of freedom, which is used to simulate physiological systems, life support systems, as well as for radiobiological and ecological studies.

Let us consider some examples of operation of the variants of simulation models developed to date, which illustrate their capabilities to some extent.

A major study [10], based on abundant experimental and clinical data served as the basis for the simulation model of fluid-electrolyte metabolism. However, for the purpose of forecasting the results of functional tests in the course of simulating weightlessness on the ground (hypokinesia), a radical modification thereof was required. The most significant modification was consideration of transport of bivalent cations of calcium and magnesium. Figure 2 shows a comparison of model data to the results of studies conducted by A. I. Grigor'yev, G. A. Kozyrevskiy and other physiologists who participated in this work. They simulated a change as a function of time in excretion of several electrolytes after a hypertensive calcium load. We can see that simulation of excretion of bivalent cations yielded satisfactory results. The poorer results for excretion of potassium can be attributed to the vagueness of many aspects of the physiological mechanism of potassium excretion by the kidneys, which exists at the present time. Perhaps, even rather approximate simulation of processes of potassium transport will require not only description of central mechanisms of regulation thereof, but differentiated consideration of the role of different segments of the nephron, which has not yet been reflected in the model.

Orthostatic test
Time of elevation

Position	Q, ℓ/min	$1/C_1$, mm Hg	RV, ℓ
Supine	5	8	2.7
Standing	7.4	10	3.2

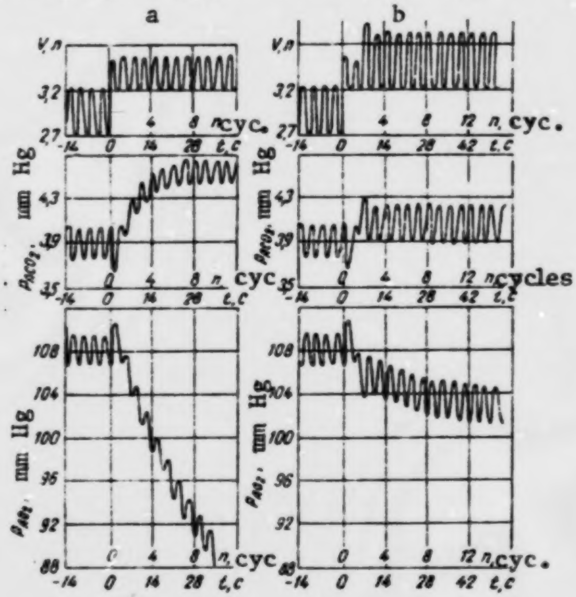


Figure 3.
Simulation of changes in parameters of respiration after orthostatic test
a) model without chemoreceptors
b) effects of arterial chemoreceptors

In studies of the influence of space flight factors on the system of external respiration, due consideration was given to the fact that they affect the most appreciably the dynamics of processes in the lungs. Accordingly, for the first time a model was developed, which rendered pulmonary gas exchange as a process in a system with rhythmically changing flow of blood and gases and the lungs as an aggregate of many functional units operating over a wide range of modes. Figure 3 illustrates the results of simulation of processes in the external respiration system during an orthostatic test. It was assumed that ascent occurs instantaneously at time t = 0. Elevation of pressure in the right atrium and increase in pulmonary blood flow Q were calcuated by means of a simulation model of circulation. Evaluation was made of increase in functional residual lung volume (RV) and decrease in elasticity of the external respiratory system ($1/C_1$), on the assumption that all these changes occur much faster than the changes in parameters of gas exchange. The curves in Figure 3 illustrate variants of simulation of the orthostatic test on the assumption of a constant chemical "drive," i.e., in the absence of afferent signal from arterial chemoreceptors and with consideration of their influence. The results of modeling indicate, in particular, that arterial chemoreceptors play an important role in stabilizing the composition of arterial blood in cases of sudden changes in parameters of the system of external respiration. The results of simulation modeling of the erythropoietic system have already been discussed in this journal [11, 12].

Thus, it is quite probable that it will be expedient, in the near future, to supplement the software presently available to medical experts with simulation models and, perhaps, algorithms of the extrapolation type. Thus, use of such models enables medical men to scan the dynamics of changes in the parameters studied within a short period of time, on the basis of assumptions of possible mechanisms of pathogenesis, and to compare various hypotheses. In addition, it is possible to evaluate parameters that are difficult to measure from the findings of observations. Simulation modeling, which combines well the advantages of heuristic medical methods and formal mathematical procedures, is very promising in our opinion, and it has undergone recent development in the United States [13].

BIBLIOGRAPHY

1. Gazenko, O. G., and Verigo, V. V. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1979, pp 3-7.

2. "Fundamentals of Space Biology and Medicine," Moscow, Vol 2, Bk 1, 1975, p 257.

3. Verigo, V. V., et al. in "Matematicheskaya teoriya biologicheskikh protsessov" [Mathematical Theory of Biological Processes], Kaliningrad, 1976, pp 202-203.

4. Pospelov, D. A. TEKHN. KIBERNETIKA [Technical Cybernetics], No 2, 1971, pp 10-17.

5. Klykov, Yu. I. "Situational Control of Large Systems," Moscow, 1974.

6. Vasil'yev, V. K., et al. KOSMICHESKAYA BIOL., No 2, 1977, pp 42-47.

7. Moiseyev, N. N., et al. EKONOMIKA I ORGANIZATSIYA PROM. PR-VA [Economics and Organization of Industrial Production], No 6, 1973, pp 39-46.

8. Akopyan, R. A. in "Voprosy kibernetiki" [Problems of Cybernetics], Moscow, Vyp 28, 1977, pp 110-117.

9. Shannon, R. "Art and Science of Simulation Modeling of Systems," Moscow, 1978.

10. Guyton, A. C.; Colman, T. G.; Granger, H. J.; et al. ANN. REV. PHYSIOL. Vol 34, 1972, pp 13-46.

11. Verigo, V. V., and Smirnova, T. M. KOSMICHESKAYA BIOL., No 1, 1978, pp 31-35.

12. Idem, Ibid, No 2, 1979, pp 13-18.

13. TRANS. ASME., Ser G, Vol 95, No 3, 1973.

EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

UDC: 612.124-057:656.7

EFFECTS OF FLIGHTS DIFFERING IN DURATION ON PROTEIN COMPOSITION OF COSMONAUTS' BLOOD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1980, pp 13-17

[Article by Ye. V. Guseva and R. Yu. Tashpulatov, submitted 3 May 78]

[English abstract from source]

After space flights of varying duration different adaptive changes in the protein composition of cosmonaut's blood were detected. A short-term 2-day flight induced a decline of gamma-globulin (immunoglobulins G and A) and β_2-glycoprotein fractions. Longer-term 16- and 18-day flights caused an increase in albumin and most globulin fractions. A long-duration 49-day flight brought about an increase in the content of C_{3c}- and C_4-factors of the complement and immunoglobulins G. A and M. Return of the blood protein composition to the normal after prolonged space flights takes a long period of time.

[Text] It is known that there was a reliable increase in total serum proteins in astronauts who had flown aboard the Apollo series of spacecraft, after their return to earth [1]. A constant increase was observed in haptoglobin, cerulloplasmin, acid α_1-glycoprotein, as well as changes in the fraction of α_2-macroglobulin. The substantial difference in the case of the 59-day mission aboard Skylab, as compared to previous flights, was retention of a constant level of blood proteins [2].

A change in blood protein synthesis, manifested by an increase in globulin fraction and appearance of a mildly positive reaction for C-reactive protein, was also observed in cosmonauts after long-term flights [3]. After the 6-day flight on the ASTP program, some increase in albumin content and decrease in globulin content, chiefly referable to gamma globulins, were demonstrated [4].

The objective of our studies included the following: 1) study of the effect of occupational training of cosmonauts on protein composition of blood and setting physiological norms for levels of different protein fractions in this group of people; 2) comparative study of the nature of changes in protein spectrum and duration of the recovery period following flights differing in duration.

We submit below the results of studying the protein composition of blood of cosmonauts who participated in flights lasting 2, 16, 18 and 49 days aboard Salyut-3 and Salyut-5 orbital stations and in their transport spacecraft of the Soyuz type.

Methods

The main protein fractions of blood serum were assayed by the method of radial immunodiffusion in M- and LC-partigenic dishes of the Beringwerk Firm (FRG), in which there were monospecific sera against blood plasma proteins in an agar-gel layer. Solutions of human blood serum containing specific amounts of the tested protein fractions were used as standards (standards of the Beringwerk Firm). We determine the amount of total blood protein by menas of the biuret reaction. The results obtained were processed by methods of variational statistics [5].

During the professional training of cosmonauts, their blood was analyzed many times in order to obtain individual background data. This made it possible to establish the range of the physiological norms for different blood proteins of 25 cosmonauts, as well as to demonstrate some typical differences in levels thereof.

Results and Discussion

The mean indices of most protein fractions of blood differed negligibly in our group of cosmonauts (see Table), and they usually presented a narrower range of fluctuation than the corresponding means of healthy people [6]. We found relatively higher mean indices for total protein and fractions of prealbumin, ceruloplasmin, α_2-macroglobulin, β-lipoprotein, transferrin and immunoglobulin D (IgD). The mean values for G_c-globulin and albumin were below and above the physiological range, respectively.

A narrower range of fluctuations between the bottom and top limit of normal was a typical finding in the protein spectrum of cosmonauts' blood, as compared to analogous indices in other healthy individuals. The higher top range of total blood protein in cosmonauts is probably attributable to the fact that the range of fluctuation of concentration of albumin, a protein that constitutes the largest fraction of all proteins assayed, was also beyond the range of mean fluctuations of this protein taken as the norm for healthy people. We demonstrated lower ranges for G_c- and C_{3c}-globulins and higher ones for α_2-macroglobulin.

We made a comparative evaluation of the data referable to 2-, 16- and 18-day (cumulative data), as well as the 49-day space flight (see Figure). Individual blood serum proteins were assayed before the flight (background values, taken as 100%), then on the 1st, 7th, 14th and 29th postflight days. We submit here only statistically reliable fluctuations of results.

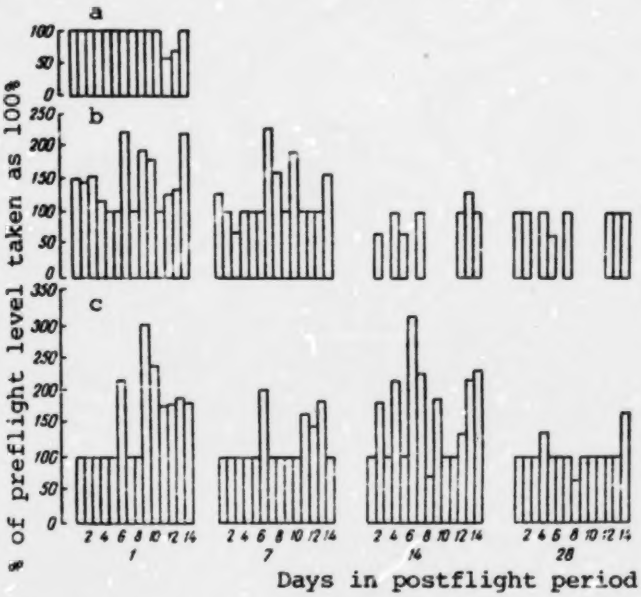
Mean indices of protein composition of cosmonauts' blood (mg/100 mℓ serum)

Protein fraction	Norm [6]		Cosmonauts	
	mean	range	mean	range
Prealbumin	25	10—40	30	27—33
Albumin	4400	3500—5500	6345	5809—6981
C-reactive protein	<1.2		<1	
β_2-Glycoprotein I	20	15—30	19	18—21
Acid α_1-glycoprotein	90	55—140	74	68—80
Ceruloplasmin	30	20—60	40	35—44
Haptoglobin	160	50—220	121	102—141
α_2-Macroglobulin	240	150—350	284	197—371
G_c-globulin	40	30—55	28	24—31
β-Lipoprotein	500	250—800	766	686—846
Transferrin	295	200—400	352	318—397
C_{3c}-globulin	110	80—140	88	77—99
C_4-globulin	30	20—50	33	29—38
IgG	1250	800—1800	1146	1052—1240
IgA	210	90—450	199	182—216
IgM	125	60—250	114	103—135
IgD	5	<15	6	3—9
Total protein	7.0	6.0—8.0	8.0	7.5—8.5
Albumin/globulin	1.9	1.8—2.0	1.9	1.8—2.0

Before the flight, the levels of blood protein fractions were within the range of the adopted norms in all cosmonauts. We only found a higher level of total blood protein and albumin. Perhaps, the high concentration of blood serum protein (mainly albumin) constitutes a protein reserve for other cells of the body. The negligible individual deviations of the blood protein spectrum were not associated with appearance of any disturbances referable to metabolic processes and immune reactions. The levels of Ig of all classes were within the usual physiological range. There was no C-reactive protein. Thus, in the preflight period we demonstrated activation only of synthesis of albumin, a protein that plays a substantial role in fluid metabolism, maintenance of osmotic pressure, transport of various ions and pigments, and performing the function of protein reserve and nutrition.

Analysis of postflight data enabled us to demonstrate some differences in the changes in blood proteins as a function of duration of space flights. It must be noted that we failed to demonstrate statistically reliable changes in β-lipoprotein, acid α_1-glycoprotein, IgD and C-reactive protein in any of the cosmonauts after the flights, and therefore data pertaining to the relevant proteins are not illustrated in the Figure.

After completion of a 2-day space flight, we observed a decline of levels of three protein fractions of blood: β_2-glycoprotein I (to 78.4%), IgG (to 57.5%) and IgA (to 67.7%). We demonstrated a decrease in IgG and IgA gamma globulin fractions, which play a vital part in immunological processes in the human body, can apparently be interpreted as the body's adaptive reaction to accelerations and weightlessness, which are factors that accompany space flights whatever their duration.



Protein fractions of cosmonauts' blood serum after 2- (a), 16- and 18- (b, total data) and 49-day (c) space flights (only statistically reliable fluctuations are shown)

1) total protein
2) prealbumin
3) albumin
4) β_2-glycoprotein I
5) transferrin
6) ceruloplasmin
7) haptoglobin
8) α_2-macroglobulin
9) G_c-globulin
10) C_{3c}-globulin
11) C_4-globulin
12) IgG
13) IgA
14) IgM

Very different changes in blood protein spectrum were observed after the 16- and 18-day flights. On the first postflight day, we demonstrated higher levels of prealbumin, albumin, as well as globulin fractions--β_2-glycoprotein I, haptoglobulin, G_c-globulin, C_{3c}-globulin, IgG, IgA and IgM--against a background of higher total protein content of blood. Such changes can be interpreted as adaptive reactions of the body to prolonged weightlessness and the set of other factors associated with the longer flight.

After the flight factors ceased to exist there was restoration of the level of most blood protein fractions within a relatively short time. Thus, only four globulin fractions were above the preflight levels on the 7th postflight day, and only IgA was above the preflight level on the 14th day. The protein composition of cosmonauts' blood became entirely normal by the 28th day of the postflight period. The only exception was the change in level of transferrin, the protein responsible for iron metabolism in the body: we found a gradual decrease in content thereof (on the 14th-28th postflight days).

After completion of the 49-day flight, we demonstrated changes only in the globulin fraction of blood. In essence, there was a change in gamma globulin fraction of proteins (IgG, IgA, IgM) and β_1-globulins (C_{3C}- and C_4-factors of the complement system), i.e., proteins involved in immune reactions. It should be stressed that we found a very high concentration of all of the above-listed blood proteins, as well as ceruloplasmin and G_c-globulin, immediately after the flight. The levels of these proteins in blood were significantly higher than the top range of the physiological norm. Probably, after 49 days of weightlessness the initial changes in protein spectrum of blood inherent in the early stages of space flights had been corrected, since the adaptation process was almost completely ended.

There appeared a tendency toward further normalization of the blood protein spectrum of cosmonauts on the 7th postflight day: only the levels of four globulin fractions remained elevated.

A drastic change in blood protein spectrum was observed on the 14th postflight day: increased levels of prealbumin and seven globulin fractions. At expressly this time, most of them reached maximum levels. The changes occurring at this stage can be interpreted as readaptation to earth after the long-term flight. We should call attention to the postflight decline (starting on the 14th day) of α_2-macroglobin level. Such changes were also found in American astronauts [1].

On the 28th day after the 49-day flight, the concentration of β_2-glycoprotein I and IgM remained high. Evidently, more time was required for normalization of these proteins.

Summarizing the results of our study of protein composition of blood of cosmonauts after they returned from flights differing in duration, it can be concluded that the least changes in functional state of the body occurred after short space flights. Space flights lasting 16 and 18 days were associated with impairment of the largest number of protein fractions. After returning from the even longer, 49-day flight, the quantitative changes in some protein fractions became even more marked, while other parameters were normalized.

These data indicate that the typical reaction of the body to prolonged exposure to space flight factors is adaptation, adjustment to new conditions, and the adaptive changes in blood protein composition in cosmonauts increase gradually with increase in duration of exposure to space flight factors (weightlessness), and they affect the maximum number of protein fractions after 16-18 days into the flight. Further increase in duration of exposure to space flight factors leads to restoration of preflight levels of some blood proteins and significant increase in concentration of others (C_{3_C}- and C_4-globulins, IgG, IgA and IgM).

On the basis of analysis of the obtained data on increase in Ig and two fractions of the complement system of cosmonauts in the postflight period (16-, 18- and 49-day missions) and data in the literature [7, 8] concerning destruction of skeletal muscles of cosmonauts in weightlessness, it was assumed that the products of atrophy of skeletal muscles could lead to synthesis of autoantibodies to striated muscles. We demonstrated similar adaptive changes in blood protein composition of polar workers after long stays under the extreme conditions of the Antarctic continent.

The established fact of postflight change in α_2-globulin fractions (haptoglobin, G_C-globulin, ceruloplasmin), i.e., the blood proteins that are actively involved in regulation of metabolic processes in the body, is also of importance. Evidently, the impaired level of blood proteins could indicate that a long-term space flight induces a substantial change in processes of protein, carbohydrate and lipid metabolism.

BIBLIOGRAPHY

1. Fisher, C. L., and Gill, C. AEROSPACE MED., Vol 43, 1972, p 850.

2. Kimzey, S. L., et al. Ibid, Vol 47, 1976, p 383.

3. Legen'kov, V. I. "Dynamics of Peripheral Blood Indices in Cosmonauts During Their Professional Training and Space Flights," author abstract of candidatorial dissertation, Moscow, 1975.

4. Gurovskiy, N. N.; Gazenko, O. G.; Yegorov, B. B.; et al. in "Kosmicheskiye polety na korablyakh 'Soyuz'" [Space Flights Aboard the Soyuz Series of Spacecraft], Moscow, 1976, p 381.

5. Ashmarin, I. P., and Vorob'yev, A. A. "Statistical Methods in Microbiological Research," Leningrad, 1962.

6. Schultze, H. E., and Heremans, J. F. "Molecular Biology of Human Proteins," New York, Vol 1, 1966.

7. Bryanov, I. I.; Yemel'yanov, M. D.; Matveyev, A. D.; et al. in "Kosmicheskiye polety na korablyakh 'Soyuz'," Moscow, 1976, p 195.

8. Tashpulatov, R. Yu.; Guseva, Ye. V.; and Petrosov, V. V. ZH. MIKROBIOL. [Journal of Microbiology], No 2, 1978, p 19.

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EFFECTS OF UNUSUAL SCHEDULES OF DAILY ACTIVITY AND SLEEP DEPRIVATION ON MAN'S FUNCTIONAL STATE AND WORK FITNESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1980 pp 17-23

[Article by A. N. Litsov and I. F. Sarayev, submitted 30 Aug 78]

[English abstract from source]

Physiological functions, work capacity and sleep characteristics of six healthy test subjects were studied for 30 days. The test subjects adhered to one of the three different regimens (1 — sleep from 2.00 a. m. to 10.00 a. m., 2 — sleep from 6.00 p. m. to 2.00 a. m., and 3 — sleep from 10.00 a. m. to 6.00 p. m.) which were aggravated by 64 hr or 72 hr vigilance during the experiment. The studies demonstrated general and specific changes in physiological functions, work capacity and sleep closely associated with the fact how far work—rest cycles were shifted and how long they were applied. Prolonged vigilance caused similar changes in physiological functions, work capacity and sleep. The test subjects showed very poor tolerance to an alteration in the work—rest cycle combined with sleep deprivation.

[Text] Plotting a daily cyclogram of man's activities on the basis of a 24-h sleep-waking rhythm is one of the main prerequisites for retaining the initial fitness for work [efficiency] and health. In this regard, the study of the distinctions of man's adaptation to different variants of sleep-waking schedules and elaboration, on the basis of these data, of optimum functional cyclograms can be considered to be one of the most important tasks for occupational medicine [1-3]. The main objective of this report is to discuss the distinctions of man's adjustment to some variants of the sleep-waking schedule, complicated by prolonged and continuous wakefulness at one of the stages of the study.

Methods

These studies* were conducted for 30 days on 6 healthy male subjects ranging in age from 28 to 42 years. There were two series of studies, in each of which three men participated concurrently. The daily cyclogram for subjects' activity in both series provided for a 24-h sleep-waking rhythm, constant 8-h watch duty shifts, each of which was taken by one subject at a time and, consequently, the first subject remained awake from 1000 to 0200 hours and slept from 0200 to 1000 hours; the second subject was awake from 0200 to 1800 hours and slept from 1800 to 0200 hours; the third subject stayed awake from 1800 to 1000 min and slept from 1000 to 1800 hours. At one of the stages of the study, each subject was scheduled for continuous duty for 64 h (first series) and 72 h (second series) without sleep. On the first daily schedule, the continuous duty was scheduled for the 3d day of the study, on the second one it was on the 13th day and on the third, it was scheduled for the 23d day.

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*These studies were conducted in collaboration with V. N. Artishuk, Yu. V. Yakushkov and Yu. A. Shpatenko.

The activities of the subjects were the same in both series, and they were strictly specified in the daily schedule, including the following: communications and radio engineering work, autonomous astronavigation, control of dynamic object, operational servicing, visual observation, testing functions of the visual analyzer, and others. In the course of the studies, we examined the circadian rhythm of some physiological functions (pulse rate, EEG rhythms), mental efficiency (simple and complex motor reactions), dynamics of higher nervous activity, dynamics of sleep (EEG stages, pulse, actogram, subjective evaluations) and behavioral reactions.

Results and Discussion

In the first series of studies, each subject followed the same work and rest schedule for 30 days (with the exception of 64 hours of continuous wakefulness). According to the obtained data, the changes in sleep-waking cycles induced signs of external and internal desynchronization of most of the indices studied in all subjects in this series (particularly on the first days); the magnitude and nature of these changes were closely related to the magnitude of phase shift in the daily cycles and effect of prolonged sleep deprivation. Thus, we see in Figure 1 that the daily pulse curves of subject F-v follow the rhythm of the new schedule, with minor deviations manifested only by some decline of amplitude of fluctuation of physiological parameters in the late evening hours, on the 3d day on the schedule that provided for a minor shift of cycles. There were also virtually insignificant deviations in the dynamics of his EEG (see Figure 1), parameters of efficiency and sleep characteristics (Tables 1 and 2).

In subject S-ko (schedule involving 5-h shift of sleep-waking cycles), the deviations of pulse parameters were more marked on the first days (see Figure 1); the EEG presented some increase in representation of θ- and δ-waves and exaltation of α-rhythm in response to stimuli, while the dynamics of psychophysiological tests were indicative of general deterioration, particularly at night. Normalization of all parameters was postponed to the 6th-7th day, and up to 12 days for some tests (see Table 1).

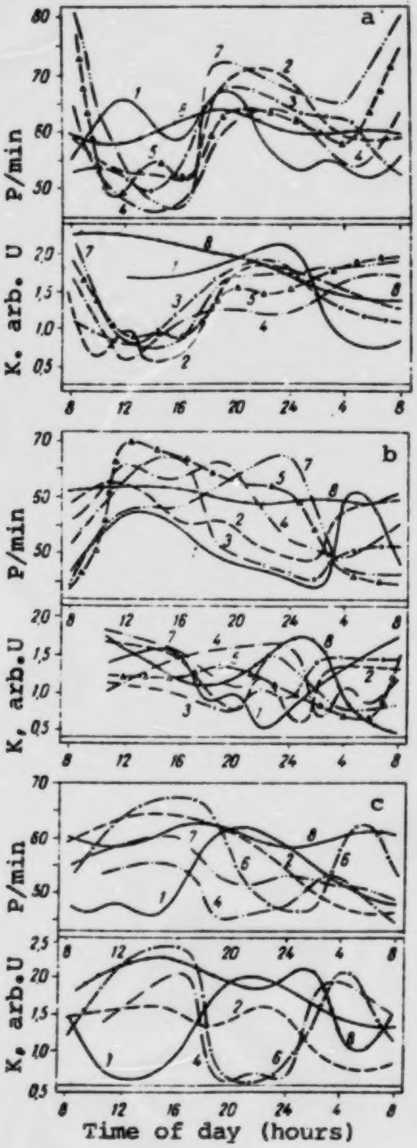

Figure 1.

24-h dynamics of pulse and EEG rhythms in first series of studies

a,b,c) subjects F-v, S-ko and B-sh

1-7) 3d, 7th-10th, 12th, 14th-16th, 20th-22d, 25th-26th, 28th-29th days of study

8) continuous wakefulness (mean data for 2 days)

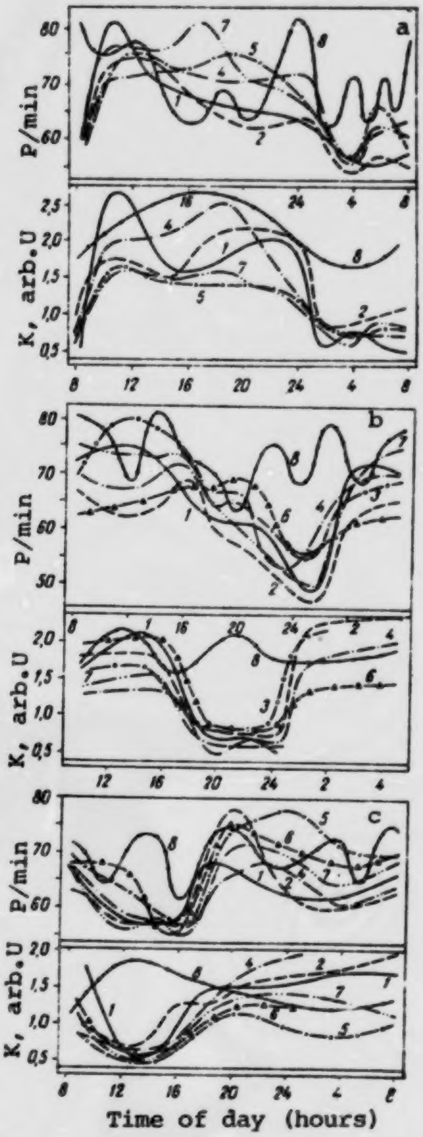

Figure 2.

24-h dynamics of pulse and EEG rhythms in second series of studies

a,b,c) subjects Kh-v, S-k and S-n

1-7) 3d, 7th, 12th, 16th, 23d-24th, 26th, 29th days of study

8) continuous wakefulness (mean data for 3 days)

In both figures: x-axis, time of day (hours); K, ratio between EEG rhythms: $\frac{\alpha+\beta}{\theta+\delta}$; arb.U, arbitrary units; P, pulse.

Sleep of S-ko was impaired, both qualitatively and quantitatively, in subject S-ko (see Table 2).

Table 1. Dynamics of efficiency indices for subjects in the first series of studies

Day of study	Waking hours	F-v			S-ko			B-sh		
		A	B	C	A	B	C	A	B	C
3	1	376	479	4.86	365	476	3,70	207	496	5,35
	4	372	562	5.14	356	526	2,79	344	596	5,33
	8	—	510	3,59	364	512	2,18	370	631	8,06
	12	341	582	5.90	275	491	2,07	418	565	6,86
6	1	365	574	3.03	330	481	2.61	272	505	5.13
	4	369	488	3.13	314	538	2,59	375	375	4,60
	8	359	449	3.53	290	527	2,68	381	536	5.87
	12	430	574	2.93	349	549	3.54	331	601	4.74
12	1	342	458	5.72	—	—	—	283	451	4,68
	4	371	498	3.31	—	—	—	307	454	4.26
	8	341	473	4.95	373	487	2,81	—	—	—
	12	377	555	6,16	338	508	3.00	—	—	—
16	1	—	—	—	365	481	2,03	306	454	2.17
	4	—	—	—	377	652	2.17	314	457	3,07
	8	444	638	2.57	288	540	2,89	—	—	—
	12	285	456	4,20	342	515	1.44	—	—	—
22	1	281	470	5.65	251	414	2.22	320	501	3.70
	4	311	468	4.64	284	450	2.12	373	480	3,42
	8	350	450	5.46	300	450	2.02	341	504	4,77
	12	336	516	4.84	296	440	2,07	331	470	3,05
26	1	370	581	5.50	330	437	2.37	303	646	3.23
	4	353	505	4.55	—	—	—	283	460	3.34
	8	356	444	4.54	288	447	2,27	410	754	2.63
	12	353	470	4.42	225	444	2.31	414	681	3,68
29	1	300	458	5.39	—	—	—	260	407	3.88
	4	283	484	4.50	—	—	—	294	487	2.82
	8	294	457	4.01	254	435	1.93	396	570	3.51
	12	388	492	6.17	310	397	1.96	361	491	3,25

Key (for this and Table 4):
A) simple motor reaction (ms)
B) reaction of choice between two alternatives (ms)
C) solving arithmetic problems (s)

Even more marked changes were noted in subject B-sh (schedule with 11-h shift of sleep-waking cycles). According to Figure 1, his daily pulse curves were distorted and flattened. The curves presented two minimums, one of which was at the usual sleep time (from 0200 to 0600) and the other corresponded to the imposed sleeping time (from 1200 to 1500 hours).

Table 2. Dynamics of sleep indices for subjects in the first series of studies

Index	F-v				S-ko				B-sh			
	days											
	1–3*	7–14*	15–22*	23–30*	1–6**	7–13**	16–22**	23–30**	1–7***	8–15***	16–23***	27–30***
Falling asleep, min	7	12	8	9	62	96	27	40	48	10	13	10
Sleep time, min	360	455	448	440	368	353	425	423	292	365	426	445
Movements per hour	3.3	3.2	3.6	3.9	5.1	5.2	4.3	6.2	4.9	5.8	5.2	5.1
% calm 5-min periods	78.0	76.0	72.6	75.0	61.5	67.5	70.0	67.3	68.4	58.2	52.8	65.2

Footnotes for this and Table 3:

*Sleep from 0200 to 1000 hours

**Sleep from 1800 to 0200 hours

***) Sleep from 1000 to 1800 hours

Restoration of typical daily dynamics was observed by the 18th-20th day. The EEG dynamics presented significantly increased representation of θ- and δ-rhythms, dysrhythmia and other disturbances in tracing pattern for a long time. On the first day, sleep was superficial, intermittent and lasted a total of about 4-5 h. Then the sleep indices gradually recovered and duration increased, reaching 7-7.5 h by the 20th-23d day (see Table 2).

Remaining continuously awake for 64 h was associated with distinct and unidirectional change in most of the parameters studied in all subjects, regardless of when the waking period began. Thus, the pulse curves for subject F-v evened out in amplitude with retention of 24-h cycle. By the end of the first and, particularly, the second day we observed a decrease in energy of α- and β-rhythms and increase in θ- and δ-rhythms. Efficiency indices worsened, particularly at night (by 50-60%). In subject S-ko, the pulse rate became the same in the daytime and at night. The EEG showed a decrease in α-rhythm and increase in θ- and δ-potentials in the early morning hours. Efficiency indices worsened mainly during the night (by 60-80%).

In subject B-sh, the curves for pulse rate retained the pattern of the new schedule during continuous wakefulness. The EEG present build-up of β_1- and β_2-rhythms, which was generally indicative of retention of a high level of wakefulness in this subject, in spite of the prolonged sleep deprivation. The latency periods of sensorimotor reactions and erroneous actions increased, reaching a maximum by the end of the second day.

Immediately after the period of prolonged continuous wakefulness, sleep improved significantly in all subjects. Time required to fall asleep was brief in all cases (1-2 min), sleep was not interrupted, being associated with minimal motor activity and prevalence of deep, slow-wave stages. On the next days, the sleep parameters of all subjects remained negligibly diminished (by no more than 5-10%). We observed rapid restoration of other parameters also. Thus, in F-v, the pulse curves conformed with the new schedule on the 2d-3d day, the EEG indices on the 1st-2d day and mental efficiency on the 3d-5th day. There was even faster readjustment of parameters in S-ko. Even less marked deviations were observed in subject B-sh.

Thus, according to the findings from the first series of studies, it can be concluded that, in the presence of an unusual work and rest schedule, at first there is desynchronization of functions and then readjustment thereof. We found that the rate of readjustment is closely related to the extent of the shift in work and rest schedule [1, 4-6].

Table 3. Dynamics of sleep indices for subjects in second series of studies

Index	Kh-v				S-k				S-n			
	days											
	1-3•	7-14•••	15-22•••	23-30•••	1-6••	7-13••	16-22•	23-30•	1-7•••	8-15•	16-23••	27-30••
Falling asleep, min	10	18	15	40	10	30	5	20	5	17	35	43
Sleep time, min	380	272	219	255	360	410	445	355	330	385	309	370
Movements per hour	6.1	9.4	7.8	8.0	6.8	5.3	6.1	8.8	6.7	8.9	8.3	7.0
% calm 5-min periods	57.5	46.2	54.0	56.0	59.0	65.1	64.0	54.3	51.3	51.2	57.0	61.2

In the second series of studies, we examined the dynamics of vital functions using 72-h continuous wakefulness followed by an 8-h shift of sleep-waking schedule. According to the data obtained (Figure 2), pulse rate conformed rather rapidly, in phase and amplitude, with the new schedule in subject Kh-v (for the first 3 days there was a 3-h shift in sleep and waking cycles). The EEG parameters and efficiency coincided almost immediately with the new schedule, and sleep became good by the 3d day, lasting a total of 7-7.5 h (see Table 3). In subject S-k (5-h shift of schedule), the pulse indices were desynchronized for the first days (flattened and distorted in phase and amplitude). The curves conformed entirely with the new schedule by the 6th-8th day. On the first days, slow θ- and δ-waves appeared on the EEG, and there was a decline in frequency of α-rhythm; these disturbances persisted for 2-3 days. Efficiency indices deteriorated according to most tests, and restoration took 8 to 12 days. On the first few days, this subject took a long time to fall asleep (up to 60-80 min); sleep was superficial and he woke up frequently. As in the first series, improvement of sleep occurred on about the 7th-12th day.

Table 4. Dynamics of efficiency indices for subjects in the second series of studies

Day of study	Waking hours	Kh-v			S-k			S-n		
		A	B	C	A	B	C	A	B	C
3	1	181	230	3.12	263	655	5.80	231	439	4.66
	4	221	596	3.09	283	616	6.30	—	—	—
	8	—	—	—	294	612	5.30	274	572	4.11
	12	277	422	4,04	311	—	5.90	260	514	3.57
6	1	209	382	2.61	317	550	5.43	165	430	3,50
	4	196	480	2.55	—	—	—	195	425	3.22
	8	223	461	2.53	390	613	5.29	182	424	3,28
	12	185	517	2,60	232	528	4.84	159	442	4,04
12	1	216	427	2.50	303	571	6.32	150	367	3.74
	4	296	339	2,30	484	460	6.20	165	337	2,86
	8	246	387	2.63	—	—	—	156	385	3,61
	12	221	317	2.99	230	—	6,04	168	410	3.17
16	1	309	414	2,42	287	655	4,56	203	356	4.09
	4	223	421	2.77	382	583	4.19	189	437	5.46
	8	288	487	2.56	364	534	5.22	285	450	3,20
	12	237	477	2,51	254	672	6,25	177	351	3,45
22	1	290	440	2.46	299	674	4.35	154	356	3,21
	4	325	456	2,69	269	646	4.35	200	442	3.13
	8	326	593	2,49	317	652	4.44	220	415	3,50
	12	292	581	2,36	419	886	4.07	190	462	3,29
26	1	272	467	2,51	208	490	4.08	135	323	3,44
	4	224	412	2,35	220	616	4.89	204	331	2,83
	8	212	422	2.63	348	582	5.22	—	—	—
	12	235	327	2,64	177	637	6,29	221	347	2,60
29	1	221	452	2,90	192	675	4,26	186	387	4,16
	4	189	391	2,51	201	632	3,88	202	436	3,71
	8	206	411	2,52	213	—	4,33	—	—	—
	12	239	444	2,60	168	578	4,67	217	431	3,86

The results on subject S-n were somewhat different from the indices for other subjects; his work and rest schedule was changed every 4-5 days (see Figure 2). The daily cycle was disrupted in this subject with each change of schedule and then it was restored; recovery became more difficult after each change of schedule. The EEg was characterized by rapid adjustment to the new schedule at first, but then there was gradual appearance of signs of persistent deviations: build-up in representation of slow waves, exaltation of α-rhythm, appearance of marked EEG dysrhythmia and others. Analogous changes were also noted in dynamics of efficiency indices (Table 4), which were also characterized by marked fluctuation [undulance] and severe deterioration in the daytime and improvement (distortion) at night. This subject present significant disturbances in dynamics of sleep.

The dynamics of the indices studied (24-h cycles, efficiency) changed during 72-h continuous wakefulness in about the same way as in the preceding series of studies.

Immediately after continuous wakefulness, all subjects in this series slept well (in spite of the new schedule), fell asleep rapidly, with low motor activity and somewhat increased number of deep slow-wave stages. Sleep lasted a total of up to 8-8.5 h. On subsequent days, the parameters changed drastically in all subjects. Thus, in Kh-v (schedule involving 11-h shift of sleep-waking cycles) the daily pulse curves retained their stereotype for the first few days (latent readjustment stage), then flattened and became distorted (stage of visible readjustment), and it is only toward the end of the study period that they conformed closer to the new schedule. EEG dynamics presented stable disturbances (slow waves, dysrhythmia, exaltation) for a long time. Efficiency indices improved immediately after the period of prolonged wakefulness (latent period of readjustment) and then worsened, the maximum changes occurring by the 22d-26th day of the study. There was also significant impairment of sleep during this period in this subject.

In spite of the use of a close to normal sleep-waking schedule after deprivation of sleep, subject S-k presented marked deviations of most of the parameters studied: circadian rhythm of pulse rate, dynamics of efficiency and sleep characteristics, which persisted almost to the end of the study (see Figure 2, Tables 3 and 4).

Thus, according to the results of the second series, the changes in dynamics of physiological functions, efficiency parameters and sleep dynamics were more marked than in the first series.

To sum up the findings as a whole, it can be concluded that man's adjustment to a new sleep-waking schedule is a rather complex process that consists of several stages [4-6]. At the same time, our studies revealed that there is a distinct correlation between readjustment of the human body and magnitude of shift in sleep-waking cycles, time and number of changes from one schedule to another. We found that prolonged sleep deprivation affected the dynamics of readjustment of physiological functions and efficiency. It was established that man tolerates the use of the same types of schedules under conditions of prolonged sleep deprivation much better. The change in sleep-waking schedules combined with prolonged sleep deprivation was tolerated much worse by the subjects and had an adverse effect on their functional state and efficiency. Such schedules should be used with great caution.

BIBLIOGRAPHY

1. Alyakrinskiy, B. S. "Fundamentals of Scientific Organization of Cosmonaut Work and Rest," Moscow, 1975.

2. Nicholson, A. AEROSPACE MED., Vol 43, 1972, pp 253-257.

3. Strugholod, H. APPL. NECH. [sic] REV., Vol 22, 1969, p 1339.

4. Kuznetsov, O. N.; Lebedev, V.I.; and Litsov, A. N. in "Problemy inzhenernoy psikhologii" [Problems of Engineering Psychology], Moscow, Vyp 1, Pt 2, 1968, pp 262-267.

5. Litsov, A. N. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1969, pp 59-65.

6. Higgins, E. A.; McKenzie, G. M.; Vaughan, G. A.; et al. in "Aerospace Medical Association Annual Scientific Meeting Preprints," San Francisco, 1975, pp 37-38.

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EFFECTS OF LONG-TERM SPACE FLIGHTS ON REACTIONS OF ADRENAL CORTEX AND MEDULLA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1980 pp 24-27

[Article by R. Kvetnyanski, R. A. Tigranyan, T. Torda, D. Repchekova, Ye. Yakhnova and K. Murgash, submitted 16 Jan 78]

[English abstract from source]

Concentrations of corticosteron and catecholamines, and activities of catecholamine synthesizing enzymes, tyrosine hydroxylase, dopamine-β-hydroxylase and phenyl ethanol amine-N-methyl-transferase, were measured in the adrenals of rats flown for 19.5 days aboard the biosatellite Cosmos-782, synchronous and vivarium control animals sacrificed on R+0 and R+26 days. The flown rats showed a moderate but significant increase in the adrenal weight, corticosteron concentration and tyrosine hydroxylase activity on R+0 day. These parameters returned to the normal on R+26 day. This data gives evidence that the adrenocortical and sympathoadrenal systems were not significantly stimulated by the space flight effects; therefore, weightlessness cannot be considered as a potent stressful agent, although its some stressogenic effect has been documented.

[Text] It has been established by numerous studies that activation of the adrenosympathetic and adrenocortical systems is one of the main symptoms of a stress reaction. Our objective here was to study the stressogenicity of long-term space flights to rats, on the basis of assaying corticoids, catecholamines and enzyme-synthesizing catecholamines in the adrenals.

Methods

We examined male Wistar-SPF rats 6-10 h and 26 days after a 19.5-day flight aboard the Cosmos-782 biosatellite.

The results obtained on flight rats were compared to the findings on two other groups of animals--intact (control) and from synchronous experiment, in which all flight conditions, with the exception of weightlessness, were simulated on the ground.

After decapitating the rats, the adrenals were rapidly extracted, cleaned, weighed and frozen in liquid nitrogen. They were stored in a frozen state for 6-12 days. As shown by studies conducted before the space flight, this period of storage of samples in a frozen state did not have an appreciable influence on the parameters measured.

The left adrenal was homogenized in 600 μℓ 0.25 M saccharose. To 100 μℓ homogenate we added 2.4 μℓ 0.4 N $HClO_4$ to precipitate proteins, and the supernatant was used to assay epinephrine and norepinephrine using a modification of the method of Euler and Lishajko [1]. The remainder of the homogenate (500 μℓ) was centrifuged under refrigeration for 20 min at 10,000 G, and we took 200 μℓ of the supernatant to assay tyrosine hydroxylase (TH) activity by the radioisotope method of Nagatsu et al. [2], and 50 μℓ for measurement of activity of phenylethanolamine-N-methyltransferase (PNMT) by the method of Axelrod [3].

The right adrenal was homogenized with 1 mℓ 1% Triton-X in 0.05 M tris-Hcl buffer (pH 7.4). To determine the activity of dopamine-β-hydroxylase (DBH) we took 150 μℓ homogenate, diluted it in the above buffer so that 100 μℓ would contain 0.4 mg adrenal tissue, centrifuged it 1 day later at 4°C and 10,000 G, and determined DBH activity in 100 μℓ supernatant according to Molinoff et al. [4]. Of the remaining homogenate, we used 350 μℓ to assay corticosterone in the adrenals by the modified method of Guillemin et al. [5].

Results and Discussion

We found enlargement of the adrenals in rats sacrificed immediately after landing, as compared to intact animals and the synchronous group (Figure 1). The concentration of corticosterone in the adrenals of flight rats did not differ reliably from the indices of intact animals, although it was reliably higher than in the synchronous group (Figure 2). Neither the weight of the adrenals nor concentration of corticosterone differed from the control in rats sacrificed 26 days after landing.

We observed a tendency toward decrease in epinephrine content of the adrenals of flight rats, as compared to the control, but there was no reliable decrease; the same tendency was demonstrated in rats of the synchronous group (Figure 3). There was also no change in norepinephrine content of the adrenals of flight animals, as compared to the other groups. The concentration of catecholamines in the adrenals showed no appreciable change from the levels for different groups 26 days after landing, although it was generally higher.

TH activity was reliably higher in the adrenals of flight rats decapitated immediately after landing, as compared to intact animals and those in the synchronous experiment (Figure 4). TH activity was restored to the control level 26 days after the space flight.

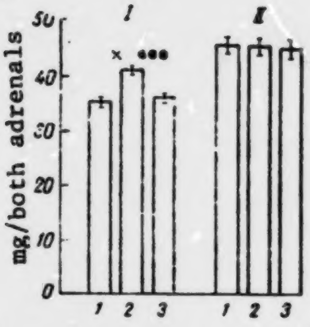

Figure 1.
Weight of rat adrenals. X's indicate statistical reliability in relation to control group ($P<0.05$); the 3 dots refer to the same in relation to synchronous group ($P<0.01$)

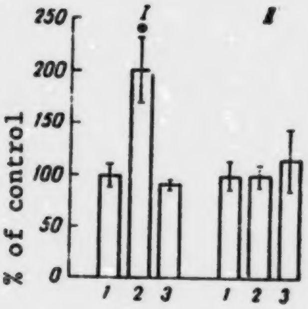

Figure 2.
Corticosterone concentration in rat adrenals. The results are given as percentage of control (control is 8 μg/g tissue); the dot indicates statistical reliability in relation to synchronous group ($P<0.05$)

In Figures 1-4, the results are given as M±m (data for 4-5 animals), and the following key applies:

I) immediately after landing of Cosmos-782 biosatellite
II) 26 days after landing of the biosatellite
1) control 2) flight 3) synchronous experiment

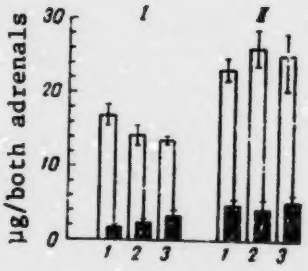

Figure 3.
Catecholamine content of rat adrenals. White columns, epinephrine; black ones, norepinephrine

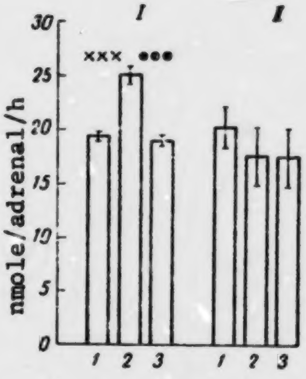

Figure 4.
TH activity in rat adrenals. The 3 x's refer to statistical reliability in relation to control ($P<0.01$) and 3 dots, in relation to synchronous group ($P<0.01$)

DBH activity increased immediately after landing in the adrenals of flight rats, as compared to both control groups; however, in view of the small number of animals examined (5 rats), the increase was unreliable. DBH activity was on the level of control values 26 days after landing. No appreciable change in PNMT activity was demonstrable in the adrenals of rats in the flight group.

As we know, activation of the rat adrenal cortex is manifested by increased secretion of corticosterone and level thereof in the adrenals, as well as increased weight of the adrenals in the case of a prolonged action. In flight rats we found a reliable icnrease in weight of the adrenals and concentration of corticosterone in them, as compared to animals in the synchronous control. After a 22-day flight aboard Cosmos-605 biosatellite, an increase in weight of adrenals and size of nuclei in the fascicular zone of the adrenals was also observed in rats [6]. However, as compared to other models of stress, the increase in corticosterone content of the adrenals of flight rats was less marked, as also indicated by the fact that there was no reliable increase in corticosterone in adrenals of flight animals, as compared to the control. A reliable increase in concentration of corticosterone in the adrenals was demonstrated, for example, in rats submitted to traumatization in a Noble-Collip drum [7] and after immobilization [8]. However, it must be borne in mind that, in our experiment, the animals were decapitated 6-10 h after landing, which is a long enough time for termination of acute activation of the adrenal cortex during the landing maneuver. On the other hand, this effect may be related to the manipulations on the animals before they were sacrificed. However, the increase in weight of the adrenals, which required longer exposure to the stress factor, may indicate that not only the landing maneuver but, perhaps, weightlessness for 19.5 days of the flight activated the adrenal cortex.

There was no reliable change in catecholamine content of the adrenals of flight rats. Epinephrine level presented a tendency toward decline, as compared to the control. This finding can be attributed either to the negligible intensity of the stressogenic factor, or increased synthesis of catecholamines in the adrenals under the influence of a long-term impulse. A decline in concentration of catecholamines in the adrenals had been observed following acute immobilization [9]; after 3 weeks of daily immobilization (which corresponds in our study to the period spent in space), the epinephrine content was no longer low, and there was an appreciable increase in norepinephrine content of the adrenals of rats submitted to stress [9].

In order to find an answer to this question, we determined the activity of enzyme-synthesizing catecholamines, higher levels of which (mainly TH) are indicative of intensified catecholamine metabolism. We found a reliable increase in TH activity in the adrenals of flight rats, as compared to the control and synchronous groups, which may be indicative of prolonged stimulation of the adrenal medulla, not only during landing and the period between landing and decapitation of the rats, but during the space flight.

There was also an increase in activity of adrenal DBH in the flight rats; however, in view of the small number of animals in the groups (5 in each), this increase is only on the borderline of reliability. PNMT activity of the adrenals did not change under the influence of the space flight, and this may be the result of insignificant stressogenicity of this factor, i.e., insufficient activation of the hypophysioadrenocortical axis, on which the increase in PNMT activity depends significantly [10, 11]. TH and DBH were already on the control level 26 days after landing. It was demonstrated that, under the influence of stress, the increased metabolism of the protein of TH reverted to normal 1-2 weeks after immobilization, i.e., the half-time for drop in activity constituted about 3 days [12]. Chuang et al. [13] cite the same half-time for decline of TH activity after cold stress.

An increase in activity of enzyme-synthesizing catecholamines was observed following various stress factors [10, 12, 14-16]. Repeated immobilization led to 2-4-fold increase in TH and DBH activity in rat adrenals [17]. Weightlessness lasting for 19.5 days of the space flight also caused a reliable increase in adrenal TH activity, but only by 25%, while DBH activity did not increase reliably.

The above data warrant the conclusion that weightlessness has an insignificant but statistically reliable effect on activation of the adrenosympathetic system of rats.

BIBLIOGRAPHY

1. Euler, U. S. V., and Lishajko, F. ACTA PHYSIOL. SCAND., Vol 51, 1961, pp 348-355.

2. Nagatsu, T.; Levitt, M.; and Udenfriend, S. ANALYT. BIOCHEM., Vol 9, 1964, pp 122-126.

3. Axelrod, J. J. BIOL. CHEM., Vol 237, 1962, pp 1657-1660.

4. Molinoff, P. B.; Weinshilboum, R.; and Axelrod, J. J. PHARMACOL. EXP. THER., Vol 178, 1971, pp 425-431.

5. Guillemin, R.; Clayton, G. W.; Lipscomb, H. S.; et al. J. LAB. CLIN. MED., Vol 53, 1959, pp 830-832.

6. Portugalov, V. V.; Savina, Ye. A.; Kaplanskiy, A. S.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1976, pp 19-25.

7. Mikulaj, L., and Kvetnansky, R. PHYSIOL. BOHEMOSLOV., Vol 15, 1966, pp 439-446.

8. Mikulaj, L., and Mitro, A. in "Neurohumoral and Metabolic Aspects of Injury," New York, 1973, pp 631-638.

9. Kvetnansky, R., and Mikulaj, L. ENDOCRINOLOGY, Vol 87, 1970, pp 738-743.

10. Kvetnansky, R. in "Frontiers in Catecholamine Research," New York, 1973, pp 223-229.

11. Wurtman, R. J., and Axelrod, J. J. BIOL. CHEM., Vol 241, 1966, pp 2301-2305.

12. Kvetnansky, R.; Weise, V. K.; and Kopin, I. J. ENDOCRINOLOGY, Vol 87, 1970, pp 744-749.

13. Chuang, D.; Zsilla, G.; and Costa, E. MOLEC. PHARMACOL., Vol 11, 1975, pp 784-794.

14. Axelrod, J.; Mueller, R. A.; Henry, J. P.; et al. NATURE, Vol 225, 1970, pp 1059-1060.

15. Kvetnansky, R.; Gewirtz, G. P.; Weise, V. K.; et al. MOLEC. PHARMACOL., Vol 7, 1971, pp 81-86.

16. Maengwyn-Davies, G. D.; Johnson, D. G.; Thoa, N. B.; et al. PSYCHOPHARMACOLOGIA (Berlin), Vol 28, 1973, pp 339-350.

17. Pfeifer, W. D. in "Catecholamines and Stress," ed. by E. Usdin, R. Kvetnansky and I. J. Kopin, Oxford, 1976, pp 265-270.

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CARDIOVASCULAR REACTION TO PERIODIC HEAD-PELVIS ACCELERATIONS ON A SHORT-ARM CENTRIFUGE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 1, 1980 pp 27-31

[Article by I. F. Vil'-Vil'yams and Ye. B. Shul'zhenko, submitted 24 Jun 77]

[English abstract from source]

As a result of 370 experiments in a 2 m-arm centrifuge, high human tolerance to acceleration of +0.8, 1.2 and 1.6 G_z (at the level of feet) was demonstrated. Cardiovascular reactions depended on the value, duration and frequency of acceleration exposures. Cardiovascular responses included, primarily, changes in regional circulation of the legs.

[Text] At the present stage of development of space medicine, there is discussion of the possibility of simulating gravitational loads by means of an onboard short-arm centrifuge (SAC) for the purpose of preventing the effects of deconditioning of the body during long-term weightlessness. It is known that rotation on an SAC under hypokinetic conditions increased man's orthostatic stability according to the index of frequency of syncopes [1]. However, the physiological effects of accelerations with a high gravitation gradient, which occur during rotation on an SAC, have been little-studied. The foreign research in this direction deals mainly with man's endurance of single exposure to accelerations with a high gravitational gradient [2, 3]. At the same time, it is considered expedient, in developing regimens for preventive rotation on an SAC, to provide for the possibility of periodically repeated use thereof.

Our objective here was to investigate the reactions of the cardiovascular system to various modes of periodic exposure to head-pelvis accelerations on an SAC.

Methods

A total of 370 tests were made with the participation of 14 healthy male volunteers using a centrifuge with a 2-m arm [radius]. The subjects were in supine position on the centrifuge platform, the Z axis coinciding with the radius of rotation, and the magnitude of the latter depended on the height of the subject, constituting a mean of 1.74 m. The axis of rotation traversed the bridge of the nose on eye level. Head-pelvis accelerations of 0.8, 1.2 and 1.6 G_z were generated at foot level. The resultant accelerations constituted 1.3, 1.6 and 1.9 G_z, respectively. The gravitational gradient over the body constituted 100% according to estimates made by the method in [2]. In order to minimize the vestibular effects of Coriolis accelerations, the subject's head was immobilized, motor activity and flow of visual stimuli were limited (housing over the head portion of the centrifuge, rotation in a darkened room).

Three series of studies were conducted. The first series (121 cases) was methodical [?]; in the second and third series (249 rotations), the subjects were submitted to accelerations varying in frequency, 2 and 3 times a day (see Table), during 3-day immersion based on the principle of "dry" submerging [4]. In order to maintain the same overall duration of exposure to accelerations during the day (120 min), the duration of rotation varied in the second and third series.

In all of the studies, we recorded the EKG in the leads of Neb followed by estimation of heart rate (HR) and photoplethysmograms (PPG) of the vessels of the ear lobe. In the third series and, partially, in the second, we recorded the PPG of vessels of the first toe and determined systemic arterial pressure (AP) in the brachial region according to Korotkov sounds and tachooscillograms.

All of the data were submitted to processing by the method of variation statistics of Student-Fisher. The differences were considered reliable at $P<0.05$.

Results and Discussion

These studies revealed that the human body is highly resistant to accelerations with a steep gravitational gradient over the body. Only in 9 of the 370 cases (2.4%) was rotation on the SAC stopped prematurely because the subjects felt poorly, complaining of general weakness and unpleasant sensations in the epigastric region. In eight cases, these subjective feelings coincided with development of cardiac dysrhythmia in the form of relative bradycardia, which preceded a decrease in PPG amplitude of ear lobe vessels to 25-30% of the base level. In one case, rotation was stopped because of appearance of multiple left ventricle extrasystoles.

Conditions under which tests on SAC were conducted

Series of studies	$+G_z$ accelerations				Number of subjects	Rotations for each subj.	Number of tests
	units	duration, min	frequency per day	intervals, h			
II	0,8	60	2 times	10 & 12	6	6	36
	1,2				6	6	36
	1,6				4	6	24
III	0,8	40	3 times	6,6 & 9	5	9	45
	1,2				6	9	54
	1,6				6	9	54

The changes in parameters of the cardiovascular system were closely linked with the magnitude and duration of accelerations (Figure 1). Maximum changes were noted during the last minute of the plateau with the maximum tested acceleration of $+1.6\ G_z$ (Figure 2). Under these conditions, HR increased by 29-47%, as compared to the base level. The HR increment at $+1.6\ G_z$ was 2-3 times greater than the changes in this parameter at $+0.8\ G_z$ ($P<0.05$). There was a mean 34-36% decrease in amplitude of ear lobe PPG by the end of the $+1.6\ G_z$ plateau, which is 1.5-2 times greater than the change in this parameter at $+0.8\ G_z$. It is important to note that there was a highly inverse correlation between dynamics of HR and ear lobe PPG amplitude at accelerations of 1.2 and $1.6\ G_z$ ($r = -0.721$ to 0.881).

The amplitude of foot vessel PPG at $0.8\ G_z$ did not change, as compared to base data, and even increased in some subjects. At $1.6\ G_z$, we observed a decrease in amplitude of foot vessel PPG by a mean of 45% toward the end of the plateau. In some subjects, the foot PPG amplitude sometimes dropped down almost to the base line. This was associated with significant changes in configuration of the pulse wave (Figure 3), which were indicative of a significant increase in peripheral resistance to blood flow and appearance of a so-called phase of retrograde blood flow in arteries [5]. These changes in amplitude and configuration of foot vessel PPG sometimes coincided with sensations of increasing heaviness of the lower limbs. In one subject, we observed massive confluent hemorrhages in the region of the lower legs and feet after a marked decline in amplitude of foot vessel PPG (during ninth rotation in the mode of $+1.6\ G_z$ for 40 min, 3 times a day).

Diastolic AP rose at all levels of accelerations and pulse AP dropped (see Figure 1). However, these changes were considerably less marked than the changes in parameters of regional circulation.

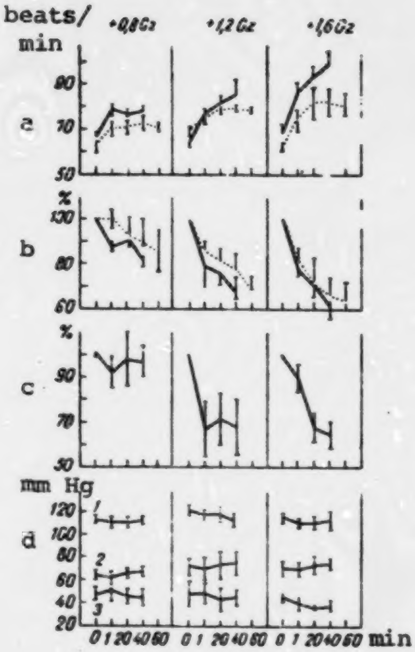

Figure 1.
Dynamics of indices of the cardiovascular system with exposure to accelerations of +0.8, 1.2 and 1.6 G_z on SAC. Mean values for all rotations

a) HR index
b) ear lobe PPG amplitude
c) 1st toe PPG amplitude
d) AP index: 1) systolic
2) diastolic
3) pulse

Here and in Figure 4, the dotted line refers to the indices in the case of rotation twice a day and solid line, three times a day

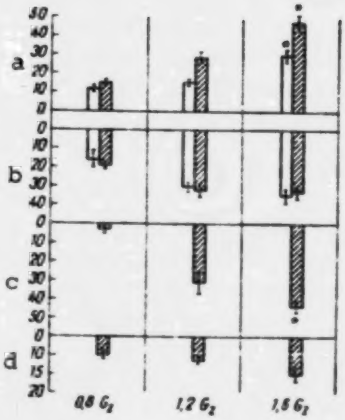

Figure 2.
Changes in indices of the cardiovascular system with exposure to accelerations of +0.8, 1.2 and 1.6 G_z on SAC. Mean data comparing the base values to the last minute of the plateau (Δ%)

a) HR index
b,c) PPG amplitude, for ear lobe and foot
d) pulse AP

White columns, indices with rotation twice a day; striped columns, three times a day. Asterisks indicate $P<0.05$ as compared to +0.8 G_z

The observed distinctive features of changes in indices of the cardiovascular system in the case of long-term exposure to accelerations on the SAC in the range of +0.8-1.6 G_z were apparently attributable to the marked nonuniformity of distribution of the accelerations over the body. While they were relatively nil at the level of the head, they reached maximum values in the region of the feet. This most probably led to a marked increase in filling of vessels of the lower extremities, as indicated by the increase in amplitude of foot PPG in some subjects exposed to 0.8 G_z. As the magnitude and duration of accelerations increased, there was apparently substantial elevation of hydrostatic pressure in both the arterial and venous parts of the vascular system of the legs and feet, with appearance of signs of venous stasis in the lower limbs.

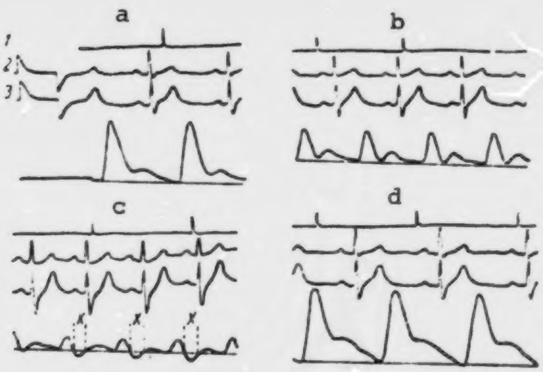

Figure 3.
Dynamics of indices of the cardiovascular system with exposure of subject S. to +1.6 G_z accelerations for 40 min on SAC. X's and dotted lines refer to "retrograde blood flow phase" (explained in the text)

a) background
b,c) plateau of +1.6 G_z, 1st and 40th min, respectively
d) 1st min of aftereffect
1) 50 mm/s paper feed rate
2,3) EKG in D and A leads of Neb calibration 1 mV = 1 cm
4) PPG of first toe with base line

The changes in the cardiovascular indices during rotation were also related to the frequency of exposure to accelerations. Analysis of HR dynamics as a function of sequential rotation number enabled us to demonstrate different tendencies of changes in this parameter in the second and third series of tests (Figure 4). In the second series, we observed two phases of change in this index with all tested modes: insignificant increase in HR from the first to third rotation, and relative stabilization between the fourth and sixth. Such dynamics of HR in the tests with rotation twice a day were probably attributable to signs of adaptation of the body to repeated exposure to accelerations at this frequency. In the third series of studies, we found a tendency toward progressive increase in HR from the first to ninth rotation. The mean HR between the sixth and ninth rotations differed reliably from the level at the first rotation ($P<0.05$). Also of interest is the fact that the mean HR with accelerations of 1.2 and 1.6 G_z and overall values of HR in all modes of tested twice a day cycles differed with statistical reliability with the last (sixth) rotation ($P<0.01$) from the values of HR with the same number of rotations in analogous modes with a periodicity of three times a day. At the same time, when we compared HR after 1-5 rotations, we failed to demonstrate reliable differences between these series. The HR dynamics observed in the third series were attributable to cumulative effects of repeated rotation on the SAC with the three-phase cycle.

Thus, in spite of the same values (+0.8, 1.2 and 1.6 G_z) and same total time of exposure to accelerations in 1 day (120 min) and during 3-day

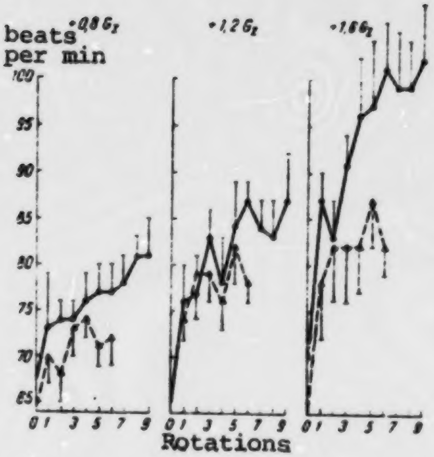

Figure 4.
HR dynamics with exposure to +0.8, 1.2 and 1.6 G_z accelerations, and mean HR in all modes as a function of sequential rotation number on SAC. The asterisk refers to $P<0.05$ (as compared to first rotation)

immersion (360 min), there was a substantial difference in HR dynamics with the two- and three-phase cycles. This indicates that it is not so much the magnitude of the gravitational impulse (product of magnitude of acceleration and rotation time) as the interval between rotations that is the decisive factor for development of adaptation and cumulative effects in the case of periodic exposure to low-level accelerations on an SAC in the range of +0.8-1.6 G_z.

Thus, as a result of these studies, we demonstrated high resistance of the human body to prolonged head-pelvis accelerations with a high gravitation gradient over the body in the range of 0.8-1.6 G_z. Predominant changes in regional circulation in the lower extremities was the typical distinction of reactions of the cardiovascular system to low-level accelerations with a high gravitation gradient. The changes in cardiovascular indices with periodic exposure to accelerations on the SAC were closely related to the magnitude, duration and frequency of exposure, as well as individual distinctions of regulatory mechanisms of the cardiovascular system.

The obtained data pertaining to substantial differences in extent of change in indices of the cardiovascular system with exposure to low levels of $+G_z$ accelerations on the SAC, differing by tenths of a G, can be used to find optimum modes of rotation for an onboard centrifuge.

BIBLIOGRAPHY

1. White, W. J. in "Symposium on the Role of the Vestibular Organs in the Exploration of Space, 1st, Proceedings," Washington, 1965, pp 209-213.

2. Piemme, T. E.; Hyde, A. S.; McCally, M.; et al. AEROSPACE MED., Vol 37, 1966, pp 16-22.

3. Nyberg, J. W.; Grimes, R. H.; and White, W. J. Ibid, pp 665-668.

4. Shul'zhenko, Ye. B., and Vil'-Vil'yams, I. F. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1976, pp 82-84.

5. Folkow, B., and Neil, E. "Circulation," Moscow, 1976.

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REACTION OF HUMAN BLOOD TO CHRONIC EXPOSURE TO LOW DOSES OF CARBON MONOXIDE IN A CONFINED ENVIRONMENT

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[Article by V. V. Zhuravlev, Z. M. Karelina, Ye. I. Nikitin and V. P. Savina, submitted 28 Feb 78]

[English abstract from source]

Morphology, biochemistry and acid—base equilibrium of blood of test subjects during their chronic exposure to low doses of carbon monoxide in an enclosed environment have been studied.

[Text] Carbon monoxide is one of the components that always pollutes the air environment of sealed compartments, in particular spacecraft. Diverse equipment, polymers and, finally, man himself may be the source of discharge of carbon monoxide [1, 2].

Most authors who have studied the toxic effect of carbon monoxide on animals and under industrial conditions on man detected specific changes in morphology and biochemistry of blood [3-9]. However, these works dealt mainly with the study of brief exposure to high concentrations of carbon monoxide.

In the first studies of the chronic effect of low concentrations of carbon monoxide [10, 11], functional disturbances of the animal nervous system were investigated. Subsequently, a number of authors [12-14] confirmed the possibility of chronic carbon monoxide poisoning with exposure to doses on the level of the maximum permissible concentrations.

Our objective here was to study the effect of long-term exposure to carbon monoxide in concentrations of 10-20 mg/m^3, against the background of the aggregate of all factors inherent in staying in a restricted, sealed compartment.

Our objectives also included the study of the effects of carbon monoxide in the presence of worse microclimate (simulation of accident [emergency] situations).

Methods

These studies involved the use of a 24 m^3 sealed chamber in four tests lasting 30 to 90 days. Four volunteer subjects, ranging in age from 23 to 36 years, participated in each study. In each of the last two tests, we simulated two "accident situations" with more difficult living conditions for 24 h (Table 1). For the analyses, we used blood taken from the finger. Blood was collected on a fasting stomach under standard conditions, on the 2d, 7th, 12th, 18th, 24th and 30th days, as well as at the end of the "accident situations." Carboxyhemoglobin content was assayed using a modified spectrophotometric method and catalase activity by the method of Bakh and Zubkova [15]. We also monitored the concentration of nonhemoglobin iron in blood serum [16]. Erythrocytes and hemoglobin were assayed by photoelectrocolorimetry using an FEK-M instrument. Blood gases and acid-base balance (ABB) were examined by a micromethod according to Siggaard-Andersen using an Astrup instrument. Tests that were conducted in the same chamber without carbon monoxide in inhaled air served as a control.

Table 1. Microclimate during tests on ordinary days (A) and days of "accident situations" (B)

Duration of study, days	A					B					
	concentration of			temp. °C	humidity, %	day of study	concentration			temp. °C	humidity, %
	CO, mg/m^3	O_2, %	CO_2, %				CO, mg/m^3	O_2, %	CO_2, %		
30	19.2—21.1	19.0—22,4	0,42—0,67	21.0—22,6	46—70						
30	14.2—16.2										
30	14,6—16,8					13	16.2	20.2	2,4	32,0	86,7
90						25	15.9	19.4	3,0	32,3	87,3
	9,5—11,0					20	46.2	21.1	3,0	34.8	91,0
						32	46.5	20.8	3.1	35,0	90,0

Results and Discussion

The subjects' blood pH was in the range of 7.36-7.41, carbon dioxide tension ($PaCO_2$) ranged from 35 to 43 mm Hg and buffer bases (BB) ranged from 47.5 to 54.7 meq/ℓ in the case of 30-day exposure to carbon monoxide in a concentration of 20 mg/m^3 with a comfortable microclimate in the pressure chamber. Standard bicarbonates (SB) and buffer base shift (BE [base excess]), which characterize the extent of metabolic changes, were in the normal range (from +1.5 to -1.5 meq/ℓ). At the end of the test, three subjects presented elevation of $PaCO_2$ to 46 mm Hg, versus the background value of 41 mm Hg (Table 2).

Table 2. Changes in blood parameters in minimum-maximum tests

Test No	CO content in chamber, mg/m³	pH	PaO₂, mm Hg	PaCO₂, mm Hg	BB, meq/ℓ	SB, meq/ℓ	SBO, meq/ℓ	O₂ saturation, %	COHb, %	Non-Hb iron, %	Catalase units	Erythrocytes, millions	Hb, g%
Initial	0,0	7,378	109,0	41,48	50,6	23,2	−0,9	97,5	3,3	124	4,46	4,12	15,2
1	19,2—21,1	7,36—7,41	100,0—130,0	35,0—46,0	47,5—51,7	21,0—24,5	+1,0—(−1,5)	97,0—98,2	11,2—11,6	146—152	3,67—3,91	3,86—4,43	14,9—17,0
2	14,2—16,2	7,35—7,40	110,0—124,0	42,0—51,0	48,0—54,5	22,8—24,5	+1,0—(−1,4)	97,4—98,1	10,4—10,6	123—125	4,03—4,21	3,82—4,37	14,3—16,6
3	11,6—16,8	7,35—7,40	94,0—118,0	38,5—50,0	42,5—52,0	22,7—27,2	+2,0—(−1,5)	96,4—97,6	10,6—10,8	123—127	3,38—3,74	3,87—4,60	14,1—15,4
	15,9—16,2*	7,36—7,39	112,0—137,0	43,5—46,0	47,0—49,0	24,2—24,6	+0,3—(+1,5)	98,2—98,4	14,6—14,8	133—135	3,39—3,78	3,69—4,12	13,2—14,7
4	9,5—11,0	7,36—7,40	92,0—110,0	44,0—54,5	48,5—58,0	24,5—27,3	+4,0—0,0	96,7—97,8	4,2—4,4	130—132	4,00—4,15	3,77—4,50	14,0—16,8
	46,2—46,5*	7,33—7,35	—	56,5—62,0	50,5—57,5	24,0—25,0	+1,5—0,0	—	17,4—18,0	156—165	2,74—2,97	3,79—4,06	14,5—15,2

*Carbon monoxide content in air of pressure chamber during "accident situation."

There were no substantial changes at the start of the study in blood morphology. We consistently demonstrated elevation by a mean of 14% of background value in level of hemoglobin starting on the 18th day. Carboxyhemoglobin content was high throughout the test period, and it constituted a mean of 11.3%. Of the other biochemical parameters studied, we should mention the increase in nonhemoglobin iron in the second half of the study, from 127 to 149 μg%, as well as a reliable ($P<0.05$) decline of catalase index from 4.46 to 3.79.

In the second study, involving exposure to carbon monoxide in a concentration of 15 mg/m^3, we found an 11.4% elevation of $PaCO_2$ on the 12th day, as compared to the background, with concurrent elevation of PaO_2 from 112 to 118 mm Hg. During this period, one of the subjects presented acidotic changes of a respiratory nature, with unsatisfactory renal compensation. By the end of the study, $PaCO_2$ was elevated in all subjects, reaching 47-54 mm Hg in some cases, while pH dropped to 7.35, which is typical of uncompensated respiratory acidosis. There was negligible change in erythrocyte count and blood hemoglobin content. Throughout the study, COHb constituted a mean of 10.5%, nonhemoglobin iron content was on the level of 124 μg% and catalase activity held at 4.12.

There was elevation of $PaCO_2$ on the first day of the third study, as a result of which some subjects presented acidotic changes of a respiratory nature. On some days, $PaCO_2$ reached 47-50 mm Hg at pH 7.35. Blood PaO_2 dropped to 12-15 mm Hg below the initial level.

When the habitat conditions were made more difficult in this study, we found normalization of acidotic changes as manifested by a drop of $PaCO_2$ to 44.4 mm Hg at pH 7.37. As a result of increased ventilation, PaO_2 rose to a mean of 125 mm Hg.

During this study, blood morphology underwent insignificant change, but erythrocyte count dropped by a mean of 12% of the base level and hemoglobin decreased from 15.1 to 13.9 g% on the 13th and 25th days. The concentration of carboxyhemoglobin increased fron 10.5 to 14.7%, while nonhemoglobin iron increased on the 25th day from 122 to 134 μg% under the more difficult conditions. The catalase index remained virtually unchanged in this study.

Studies of ABB in the first half of the fourth study consistently revealed changes in all subjects inherent in respiratory acidosis varying in degree of compensation. On some days $PaCO_2$ reached 55 mm Hg. In some cases, metabolic disturbances of ABB were added (BE = 4.0 meq/ℓ) to the signs of respiratory acidosis.

As a result of exposure to the more difficult habitat conditions, on the 33d day the subjects presented elevation of $PaCO_2$ to 59.0-62.0 mm Hg. The active blood reaction dropped to 7.33. From the 64th day on, there was normalization of ABB; however, $PaCO_2$ remained 10% above the background level.

The subjects' blood presented an increase in erythrocyte count, from 4.2 million to 4.41 million, and in hemoglobin, from 15.3 to 16.5 g%, from the first days of the study.

Starting on the 49th day, erythrocyte count and hemoglobin content of peripheral blood gradually decreased, constituting 3.86 million and 14.6 g%, respectively, versus base levels of 4.27 million and 15.4 g%. The COHb concentration held at 4.3% and nonhemoglobin iron at 137 μg% throughout the period of the study. During the period of worse microclimate, these parameters increased to 17.7% and 161 μg%, respectively. The catalase index changed only during the second "accident situation," when it dropped from 3.27 to 2.81.

When analyzing the obtained results, one should proceed not only from the fact that the selected concentrations of carbon monoxide exerted an influence, but that the entire aggregate of conditions inherent in sealed environments had an effect on the subjects. Along with specific changes in amount of carboxyhemoglobin and nonhemoglobin iron, and changes in activity of catalase indicative of varying degrees of carbon monoxide poisoning, we demonstrated changes in acid-base status of the human body. It should be noted that, with chronic exposure to carbon monoxide in concentrations of 10-20 mg/m^3, we demonstrated a difference only in severity of ABB disturbances, which were characterized mainly by an increase in carbon dioxide tension in blood and moderate decline of its pH. As a rule, elevation of $PaCO_2$ was associated with some elevation of blood PaO_2 which, in turn, was the result of compensatory increase in pulmonary ventilation. However, the respiratory compensation did not provide for an appropriate decline of $PaCO_2$. On this basis, it can be assumed that this phenomenon is related to diminished activity of carbonic anhydrase which is involved in decomposition of carbonic acid and elimination of carbon dioxide [17-19]. Nor can we rule out the possibility of elevation of the threshold of excitability of the respiratory center under the influence of the tested concentrations of carbon monoxide. In favor of this hypothesis is also the decline of $PaCO_2$ and normalization of acidotic symptoms on the 13th and 25th days of the third study, when the concentration of carbon monoxide in the chamber was increased, air temperature was raised and humidity increased, which led to significant increase in pulmonary ventilation. We failed to demonstrate such an effect in the fourth study, where we increased the carbon monoxide level to 46 mg/m^3, along with elevation of temperature and increase in carbonic acid in the chamber. Evidently, this concentration of carbon monoxide induced even greater changes in regulation of respiration.

In the 90-day study, where the subjects were continuously exposed to carbon monoxide in a concentration of 10 mg/m^3, the previously observed changes in ABB, erythrocyte and nonhemoglobin iron content leveled off after the subjects had spent 41 days in the tested atmosphere. Hence, the signs of carbon monoxide poisoning demonstrated at the start of the study leveled off as a result of development of adaptive reactions, and this was aided by creating comfortable conditions in the chamber. However, it must be borne in mind that, with increase in duration of the stay in the chamber and development of asthenization, there was a decrease in reactivity of the body, and the time could come when there would again be manifestation of carbon monoxide poisoning. We cannot explain at the present time the fact that greater changes are demonstrable with exposure to carbon monoxide in a concentration of 15 mg/m^3 than 20 mg/m^3, since there were too few subjects involved in our studies.

Thus, studies of the effect of carbon monoxide in concentrations of 10-20 mg/m^3 under ordinary and difficult living conditions revealed that there were ABB disturbances of an acidotic nature, as well as a change in blood levels of carboxyhemoglobin, nonhemoglobin iron and in catalase activity. The toxicity of the tested concentrations of carbon monoxide depends on the entire set of factors inherent in the environment of a sealed chamber.

BIBLIOGRAPHY

1. Sjostrand, T. NORD. MED., Vol 43, 1950, p 211.

2. Savina, V. P.; Sokolov, N. L.; and Nikitin, Ye. I. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1976, p 62.

3. Kreuzer, F., and Roughton, F. HELV. PHYSIOL. PHARMACOL. ACTA, Vol 12, 1954, p 78.

4. Dvoryaninova, N. K. in "Voprosy gigiyeny truda, profpatologii i promyshlennoy toksikologii" [Problems of Industrial Hygiene, Occupational Pathology and Industrial Toxicology], Sverdlovsk, Pt 2, 1958, p 222.

5. Stolyarchuk, N. K. in "Promyshlennaya toksikologiya" [Industrial Toxicology], Moscow, 1960, p 283.

6. Kol'kovskiy, P., and Raycheva, V. GIG. TRUDA [Industrial Hygiene], No 11, 1962, p 35.

7. Zatsepilin, A. G. in "Voprosy professional'noy patologii v osnovnykh otraslyakh promyshlennosti Luganskoy oblasti" [Problems of Occupational Pathology in the Main Branches of Industry in Luganskaya Oblast], Lugansk, 1965, p 23.

8. Zhgutov, I. I., and Khalepa, B . F. in "Dnepropetrovskiy med. in-t. Nauch. sessiya. 28-ya. Materialy" [Proceedings of 28th Scientific Session of Dnepropetrovsk Medical Institute], Dnepropetrovsk, 1965, p 72.

9. Tiunov, L. A., and Kustov, V. V. "Toxicology of Carbon Monoxide," Leningrad, 1969.

10. Gorsheleva, L. S. FARMAKOL. I TOKSIKOL. [Pharmacology and Toxicology], No 5, 1944, p 47.

11. Frolov, Yu. P. "Higher Nervous Activity in the Presence of Toxicosis," Moscow, 1944.

12. Gadaskina, I. D., et al. GIG. TRUDA, No 11, 1961, p 13.

13. Pecora, L., et al. FOLIA MED. (Naples), Vol 41, 1958, p 97.

14. Kustov, V. V.; Tiunov, L. A.; and Vasil'yev, G. A. GIG. TRUDA, No 6, 1963, p 53.

15. Pushkina, N. N. "Biochemical Methods of Investigation," Moscow, 1963, pp 195, 309.

16. Kassirskiy, I. A. (editor) "Manual of Functional Diagnostics," Moscow, 1970, p 378.

17. Korsun', A. Ya. quoted by L. A. Tiunov and V. V. Kustov.

18. Kremneva, S. A. in "Voprosy promyshlennoy toksikologii" [Problems of Industrial Toxicology], Moscow, 1960, p 104.

19. Guarino, A.; Biondi, S.; Bocculatte, F.; et al. FOLIA MED. (Naples), Vol 42, 1959, p 376.

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PROBABILITY OF ALTITUDE DECOMPRESSION DISORDERS WHEN BREATHING OXYGEN CONTAINING HUMAN WASTE GASES

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No 1, 1980 pp 36-39

[Article by A. V. Sedov, A. N. Mazin and N. A. Surovtsev, submitted 11 Jan 78]

[English abstract from source]

Probability of altitude decompression disease in a hypobaric oxygen environment containing gaseous human wastes has been explored. The development of the disease does not depend on the presence of wastes in the environment. Its frequency increases with exercises. The decrease of the barometric pressure to 308 mm Hg causes decompression disease only in the test sudjects having traumatized limbs. The frequency of the disease during further decrease in the pressure down to 198 mm Hg increases substantially.

[Text] There has been insufficient study of the problem of occurrence of altitude decompression disorders (ADD) in man as related to the chemical composition of an artificial gas atmosphere (AGA). We know of only a few studies in this field [1-4]. It was reported in them that an increase in carbon dioxide in oxygen used for breathing is involved in development of ADD. However, the oxygen used for breathing in space suits with regeneration types of life support systems usually contains not only carbon dioxide, but other human waste. According to data in the literature [5-8], such waste products as carbon monoxide, aliphatic and aromatic hydrocarbons, amines and acetone are of the greatest toxicological and hygienic significance in polluting the AGA. For this reason, it is deemed expedient to pursue studies in order to determine the correlation between incidence of ADD and degree of rarefaction of the atmosphere and levels in oxygen used for breathing of the above-mentioned human waste. Such information is needed to obtain base data to be used for development of measures to prevent ADD.

Methods

To solve this problem, we conducted studies involving 44 subjects ranging in age from 20 to 45 years. In all, we conducted 669 tests at "altitudes" of 7000 and 10,000 m. The "climb" to 7000 m was made without prebreathing. Prior to ascending to 10,000 m, the subjects breathed pure oxygen for 1 h. They reached the "altitude" of 7000 m in 1.5-2 min and 10,000 m in 2-3 min.

During the tests, the subjects breathed either pure oxygen (background data), or oxygen containing human waste: carbon monoxide (concentration of 10-300 mg/m^3), methane (150-400 mg/m^3), acetone (50-200 mg/m^3), phenol (3-9 mg/m^3) and dimethylamine (DMA, 0.5-1 mg/m^3). We also tested the effects of various combinations of oxygen and waste products: carbon monoxide, methane and phenol; carbon monoxide and DMA. We selected the concentrations of waste products on the basis of possible level of accumulation in sealed environments [9].

During the tests, the subjects either rested, or performed moderate physical work involving 5-6.5 kcal/min expenditure of energy. Upon reaching the indicated "altitude" and after recording vital physiological parameters, the subjects immediately began the physical work. This was done in cycles, on a physical load stand, where the subjects lifted a weight with the hands and feet simultaneously. The exercise cycles lasted 40 min with 20-min intervals between them. In all, the subjects performed six work cycles in the 6 h they spent at a given "altitude." Air temperature in the pressure chamber was 18-27°C and relative humidity was 40-60%. The subjects wore either cotton underwear or pressure suits. They spent 6 h at the indicated "altitude."

Onset of ADD was diagnosed according to the subjects' subjective reports. In addition, their general condition was evaluated according to the data from continuous medical monitoring.

Upon appearance of the first signs of ADD, the subjects were rapidly "brought down" hospitalized for 24 h, during which time they were submitted to comprehensive clinical examination.

Results and Discussion

The Table shows the distribution of ADD as related to experimental conditions.

This table shows that ADD occurred in 0.5% of the cases (3 out of 585 tests) when the subjects were lifted to an "altitude" of 700 m. These three cases were referable to three different subjects. For this reason, the percentage of ADD calculated in relation to subjects involved in this series of tests (44) constituted 6.8%. The observed cases of ADD were referable to the most frequently encoutnered bone and joint form (bends). After the "descent," the pains in the joints and muscles disappeared without a trace. The cases of ADD detected during the tests can be classifed, according to the classification of Gray [10] and several other researchers, as the mild stage, which is characterized by mild pain occurring mainly upon moving. Clinical examination of subjects with ADD failed to demonstrate deviations from normal with reference to functional systems. In two of the three cases of ADD occurring at the indicated barometric pressure, the subjects breathed pure oxygen and in the other, a gas mixture with methane in a concentration of 400 mg/m^3. Analysis of the cases of ADD failed to demonstrate any influence on the part of human waste gases contained in oxygen in the above concentrations on the probability of ADD. Decompression disorders were found in two subjects who performed exercises and one who remained at rest. However, when compared to the number of tests conducted under the same conditions, these cases did not enable us to demonstrate an effect of exercise on the incidence of ADD at a barometric pressure of 308 mm Hg.

Probability of ADD in subjects at barometric pressure of 308 and 198 mm Hg

Index	Barometric pressure, mm Hg		AGA								Temp. °C		Physical activity, kcal/min	
	308	198*	O_2	O_2+CO	O_2+CH_4	O_2+phenol	O_2+acetone	O_2+DMA	O_2+CO+CH_4+phenol	O_2+CO+DMA	18—12	21—27	1.5—2	5—6,5
Number of tests	585	84	334	151	84	26	43	53	41	26	448	212	84	585
Cases of ADD	3	6	5	3	1	0	0	0	0	0	5	4	2	7

*Prebreathing for 1 h.

A scrutiny of the history of these three subjects revealed the following: subject R. had had a dystrophic process in the left knee joint in the past; P-v had sustained trauma of the right ankle, while I-ko, who had skied, played soccer and hockey for 15 years, had sustained numerous traumas and contusions to the major joints. In all three cases, altitude decompression pain was localized expressly in the regions of traumatized knee and ankle joints.

The results of the tests conducted at an "altitude" of 10,000 m revealed that, in spite of 1-h prebreathing with pure oxygen, the incidence of ADD increased drastically with decline of barometric pressure and their severity increased. The incidence of ADD among subjects exposed to this barometric pressure constituted 7.1% (6 cases out of 84), or 25% in relation to number of subjects (4 out of 16 subjects participating in this series of studies). At this pressure, ADD was manifested in a more marked form and, in several cases, occurred in the form of severe muscle and joint pain. Most of the ADD cases demonstrated in this series of tests (4 cases) could be classified as the first stage of decompression disorders, according to the classification of Gray [10]. However, according to the same classification, two cases of ADD should be identified as the second stage, which is characterized by tolerable but gradually increasing pain. This pain, as in the preceding series of tests, disappeared without a trace after the subjects "descended" from the high "altitude." We failed to demonstrate a single case of third stage ADD in either series of tests.

In three of the six cases of ADD that occurred at 10,000 m, the subjects breathed pure oxygen and in the three others, oxygen containing carbon monoxide in a concentration of 15 mg/m^3. Thus, it is not deemed possible to make a judgment in this series either with respect to the effect of gas mixtures containing human waste on probability of occurrence of ADD. We were impressed by the fact that ADD occurred during performance of physical work in five cases and at rest in one. This confirms a fact that is known from the literature [11], that physical exercise is instrumental in occurrence of ADD. As in the preceding series, we failed to demonstrate any pattern of change in probability of ADD as a function of ambient temperature.

The six cases of ADD were distributed as follows: at an "altitude" of 10,000 m, ADD occurred 3 times in the same subject (D-ko), and the other 3 cases were referable to others (Ts-ch, G-v and P-n). The histories revealed that subject D-ko had had a femoral fracture, while G-v had suffered a spiral fracture of the leg; however, the other two subjects (P-n and Ts-ch) had not sustained any trauma in the past. Evidently, as was the case at an "altitude" of 7000 m, prior history plays an important role in onset of ADD at 10,000 m (4 out of 6 cases). At the same time, analysis of incidence of ADD as a function of a specific waste product and its concentration in the AGA reveaeld that these factors do not affect the probability of occurrence of this disease. Thus, there were 5 cases of ADD out of 334 when breathing pure oxygen and 4 out of 335 when breathing gas mixtures.

Thus, analysis of the obtained data enables us to conclude, with some degree of probability, that the waste products studied cannot cause development of ADD at "altitudes" of 7000 and 10,000 m in the concentrations that may be encountered in the artificial gas environment of sealed compartments. At these "altitudes," ADD occured both during performance of heavy physical labor and at rest. Analysis of the obtained data warrants the conclusion that it is imperative to conduct occupational screening of candidates for work at low barometric pressure with due consideration of their prior medical history.

BIBLIOGRAPHY

1. Genin, A. M. VOYEN.-MED. ZH. [Military Medical Journal], No 8, 1948, pp 48-51.

2. Gramenitskiy, P. M. "Conditions and Mechanism of Development of Decompression Disorders," doctoral dissertation, Leningrad, 1967.

3. Zagryadskiy, V. P.; Sidorov, O. Yu.; and Sulimo-Samuyllo, Z. K. in "Problemy kosmicheskoy meditsiny" [Problems of Space Medicine], Moscow, 1966, pp 175-176.

4. Behnke, A. R. MEDICINE (Baltimore), Vol 24, 1945, pp 381-402.

5. Gorodinskiy, S. M.; Sedov, A. V.; Mazin, A. N.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1968, pp 72-76.

6. Kustov, V. V., and Tiunov, L. A. "Toxicology of Biological Waste Products and Significance Thereof in Formation of the Artificial Atmosphere of Sealed Compartments," Moscow, 1969.

7. Nefedov, Yu. G.; Savina, V. P.; Sokolov, N. L.; et al. KOSMICHESKAYA BIOL., No 5, 1969, pp 71-77.

8. Uands, R. K. in "Osnovy kosmicheskoy biologii i meditsiny" [Fundamentals of Space Biology and Medicine], Vol 2, Bk 1, 1975, pp 74-104.

9. Sedov, A. V. in "Problemy individual'noy zashchity cheloveka" [Problems of Personnel Protection], Moscow, Pt 2, 1974, pp 3-37.

10. Gray, J. S. in "Decompression Sickness," ed. by J. F. Fulton, Philadelphia, 1951, pp 182-191.

11. Malkin, V. B. in "Osnovy kosmicheskoy biologii i meditsiny," Moscow, Vol 2, Bk 1, 1975, pp 11-73.

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EFFECT OF HYPEROXIA ON OXYGEN TRANSPORT PROPERTIES OF BLOOD

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[English abstract from source]

In 9 normal test subjects, aged 19—32, pO_2, pCO_2 and pH of arterial and venous blood were measured. The curve of oxyhemoglobin dissociation during 20 min inhalation of a 95 % O_2 containing mixture was analyzed. The studies demonstrate that during hyperoxia there is a shift to the left of the dissociation curve in native blood and standard curve (i. e. normalized to pH 7.4). This shift of the curve of oxyhemoglobin dissociation indicating an increase in hemoglobin affinity for oxygen seems to be one of the factors responsible for an increase in the pO_2 arteriovenous difference and a much lower increment of venous pO_2 than that of arterial pO_2.

[Text] The wide use in aviation and space medicine of oxygen at normal and high pressure, on the one hand, and side-effects with the use thereof, on the other [1-4], make it necessary to conduct an in-depth study of the effect of this gas on the body. Yet, many aspects of the functional state of organs and systems in the presence of hyperoxia have still not been investigated sufficiently. This applies, in particular, to the respiratory function of blood, which plays a first and foremost role in providing for oxygen homeostasis in the body.

Our objective here was to study oxygen transport function of blood in essentially healthy individuals, in the presence of hyperoxia.

Methods

We studied 9 healthy individuals ranging in age from 19 to 32 years.

They breathed a gas mixture containing 95% oxygen and 5% nitrogen from the closed system of an SG-1M spirograph for 20 min. Oxygen content of the working cylinder of the spirograph was monitored with an MMG-7 oxygen analyzer, which was connected to the spirograph at the point of attachment of the gas analyzer for determination of residual lung volume.

Before the test and in the 19th-20th min thereof, we took arterial (from brachial artery) and venous (from ulnar vein) blood to measure oxygen (pO_2) and carbon dioxide tension (pCO_2), pH, as well as venous blood to plot the curve of oxyhemoglobin dissociation. Blood was taken by puncturing vessels into a dry sterile syringe. The blood intended for measurement of gas tension and pH was transferred into a cooled test tube with 1-2 drops of heparin solution (1:5 dilution) under vaseline oil, after which the tube was put on ice and in the refrigerator. The tests were made no later than 2 h after taking blood. Blood was taken from the test tube with a syringe with a long needle, and immediately transferred to the measuring dishes [pits]. The method of taking the blood and transferring it into the measuring dish precluded its contact with atmospheric air; the pH was determined electrochemically and pO_2 polarographically by menas of a Clark electrode. The measurements were made with a micro-Astrup instrument (Denmark), type PHM-71. An ABC70 (Denmark) computer was used to calculate pCO_2 on the basis of pH value.

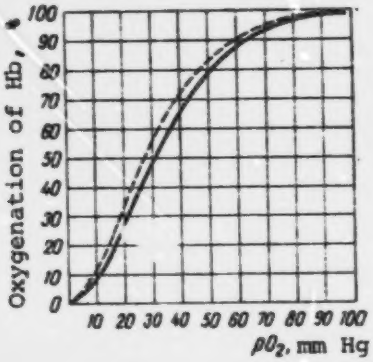
We analyzed the curve of oxyhemoglobin dissociation obtained on a DCA-1 instrument (Denmark). In order to determine the oxygen-binding properties of blood, the instructions for use of this apparatus indicate that one should determine the half-saturation points (P_{50}), i.e., the pO_2 levels at which hemoglobin is 50% oxygenated. This parameter is known as the "discharge tension" [5] and reflects the blood's capacity to give off oxygen to tissues. An increase in P_{50} signifies a shift of the curve to the right, indicative of decreased affinity of hemoglobin for oxygen, while a decrease in P_{50} indicates a shift to the left, which reflects increased affinity of hemoglobin for oxygen.

Since the DCA apparatus produces an oxyhemoglobin dissociation curve that is typical for a given batch of blood with its inherent pH, determination of P_{50} at standard pH is made in accordance with the instructions for use of the apparatus.

However, determination of P_{50} is not enough to evaluate the oxygen transport function of hemoglobin. Indeed, evaluation of level of oxygenation of hemoglobin at the most diverse levels of pO_2 appears to be substantial. For this reason, we performed the procedure, which is described above for determination of P_{50}, to find the pO_2 levels corresponding to 10, 20, 30, 40, 60, 70, 80, 90 and 100% oxygenation of hemoglobin. This enabled us to plot the standard curve of dissociation of oxyhemoglobin at a stable pH (7.4), in addition to the curve of oxyhemoglobin dissociation inherent in the actual conditions of a given blood sample with its inherent pH and pCO_2 levels. As a result, it was possible to make a differentiation, by neutralizing the blood pH changes, between the significance of intraerythrocytic factors and actual changes in hemoglobin, on the one hand, and extraerythrocytic factors in the dynamics of oxygen-binding properties of hyperoxic blood.

Results and Discussion

As shown by our studies, pO_2 levels corresponding to all analyzed levels of hemoglobin oxygenation dropped in unadulterated blood in the oxygen test. The drop of pO_2 was reliable within the range of P_{50}-P_{80}. This decline reflects an increase in affinity of blood for oxygen and a shift to the left of the curve of dissociation of oxyhemoglobin in the presence of hypoxia (see Figure).



Curve of dissociation of oxyhemoglobin in native blood in the base state (solid line) and with hyperoxia (dash line)

Studies of the standardized curve of dissociation of oxyhemoglobin revealed that the reliable shift of the curve to the left under hyperoxic conditions was retained. The pO_2 corresponding to all tested levels of oxygenation was lower than in the base state, and the decline of pO_2 was reliable in the range of P_{20}-P_{80} (see Table 1).

According to the data listed in Table 2, in addition to the distinct increase in arterial oxygen tension (p_aO_2) in the presence of hyperoxia, there was a significant increase in arteriovenous difference for pO_2, as a result of which the increase in oxygen tension of venous blood (p_vO_2) was significantly less marked than the increase in p_aO_2. Under hyperoxic conditions there was virtually no change in levels of pCO_2 in arterial and venous blood, as well as arteriovenous difference for pCO_2. Accordingly, no reliable changes were demonstrated in pH of arterial and venous blood.

Hyperoxia led to a distinct increase in affinity of hemoglobin for oxygen in the tested individuals. With reference to the mechanism of this phenomenon, we must note the following: In the first place, blood pH and pCO_2, i.e., the most important extraerythrocytic factors affecting affinity of hemoglobin for oxygen, underwent very negligible change during the oxygen test (see Table 2). In turn, the lack of changes in blood pCO_2 and pH is attributable to the virtually stable level of ventilation [6-8] and gas exchange [3, 9] under hyperoxic conditions. In the second place, with inhalation of oxygen the shift to the left of the standard curve of oxyhemoglobin dissociation persisted, i.e., the curve scaled to standard pH. Therefore, it can be stated that the increase in affinity of hemoglobin for oxygen in the presence of hyperoxia is attributable to intraerythrocytic mechanisms.

Table 1. Magnitude of shift of indices of curve of oxyhemoglobin dissociation (mm Hg) in the presence of hyperoxia, as compared to the base level

Index	Dissociation curve for OHb in nat. blood	Standard curve of OHb dissociation
P_{10}	—0,4	—0,5
P_{20}	—1,0	—1,06
P_{30}	—1,3	—1,36*
P_{40}	—1,4	—1,24*
P_{50}	—1,9	—1,69*
P_{60}	—2,0*	—1,81*
P_{70}	—2,3*	—2,2*
P_{80}	—2,4*	—2,1*
P_{90}	—2,2	—2,1
P_{95}	—1,4	—1,51
P_{100}	—3,1	—3,1

* $P<0.05$.

Table 2. Indices of gas composition (M±m) and pH of arterial and venous blood in the presence of hyperoxia

Index	Base level	Hyperoxia
Arterial blood:		
pO_2, mm Hg	95,3±4,02	252±16,09*
pH	7,38±0,06	7,383±0,152
pCO_2, mm Hg	36,1±1,02	35,3±1,93
Venous blood:		
pO_2, mm Hg	33,2±1,1	40,5±1,24*
pH	7,33±0,05	7,346±0,041
pCO_2, mm Hg	43,5±1,2	44,5±1,58
Arteriovenous pO_2 difference, mm Hg	62,3±7,18	212,9±16,4*
Arteriovenous pCO_2 difference, mm Hg	7,7±1,12	9,23±1,63

* $P<0.01$ as compared to base level.

What then is the significance of the shift to the left of the curve of dissociation of oxyhemoglobin, which was demonstrated with inhalation of oxygen?

As shown by the studies, there was an increase in arteriovenous pO_2 difference when breathing oxygen (see Table 2). We cannot attribute the increase in arteriovenous difference for pO_2 exclusively to slowing of blood flow, which is inherent in hyperoxia [10, 11], since the dynamics of arteriovenous difference for pCO_2 were insignificant (see Table 2). The higher point in the artery, at which delivery of oxygen to tissues begins, on the curve of oxyhemoglobin dissociation in the presence of hyperoxia is also important, and as a result the discharge of oxygen by hemoglobin is associated with increase in arteriovenous difference for pO_2. In the light of these data, the greater arteriovenous difference for pO_2 in the presence of hyperoxia could also be attributed to affinity of hemoglobin for oxygen, as a result of which delivery of oxygen by blood to tissues is associated with significant decline of pO_2 in blood plasma.

It could be assumed that increased affinity of hemoglobin for oxygen should lead to increased association of hemoglobin with oxygen in the lungs. However, expressly in the range of high levels of hemoglobin oxygenation (starting at 90%), there was unreliable increase in affinity of hemoglobin for oxygen. Moreover, regulation of rate of association of hemoglobin with oxygen is less significant than regulation of rate of dissociation of oxyhemoglobin. Indeed, while the rate of delivery of oxygen by blood is not high (50% oxygen given off by erythrocytes in 0.75-0.9 s) and affinity of hemoglobin for oxygen has an appreciable effect on it, association of oxygen and hemoglobin occurs 10 times faster, and 50% oxygenation of erythrocytes requires 0.08-0.09 s [12]. This rate is quite adequate for normal oxygenation of erythrocytes, and change therein within a certain range would not affect the process.

Thus, in the presence of hyperoxia there is an increase in affinity of hemoglobin for oxygen, which is manifested by a shift to the left of the curve of dissociation of oxyhemoglobin. The increase in affinity of hemoglobin for oxygen is one of the causes of the distinct increase in arteriovenous difference for pO_2 and significantly lower increment of pO_2 in venous blood than the increment of p_aO_2 during the oxygen test.

BIBLIOGRAPHY

1. Zhironkin, A. G. "Oxygen: Physiological and Toxic Effects," Leningrad, 1972.

2. Comroe, J. H.; Dripps, R. D.; Dumke, P. R.; et al. J.A.M.A., Vol 128, 1945, pp 710-717.

3. Doležal, V. PHYSIOL. BOHEMOSLOV., Vol 11, 1962, pp 142-158.

4. Matthys, U., and Buhlmann, A. A. SCHWEIZ. MED. WSCHR., Vol 100, 1970, pp 1313-1316.

5. Krogh, A., and Leith, J. J. PHYSIOL. (London), Vol 52, 1919, pp 288-300.

6. Ivanov, L. A. PAT. FIZIOL. [Pathological Physiology], No 5, 1976, pp 72-77.

7. Korkushko, O. V., and Ivanov, L. A. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1976, pp 45-50.

8. Bishop, J. M.; Harris, P.; Bateman, M.; et al. CLIN. SCI., Vol 22, 1962, pp 53-63.

9. Agadzhanyan, N. A., and Kalinichenko, I. R. in "Gory i sistema krovi" [High Altitudes and the Blood System], All-Union symposium, Frunze, 1969, pp 3-6.

10. Zhironkin, A. G.; Panin, A. F.; and Sorokin, P. A. "Effect of High Partial Oxygen Tension on Man and Animals," Leningrad, 1965.

11. Sorokin, A. A. in "Funktsii organizma v usloviyakh izmenennoy gazovoy sredy" [Body Functions in an Altered Gas Environment], Moscow--Leningrad, Vol 2, 1958, pp 46-60.

12. Rapoport, S. M. "Medical Biochemistry," Moscow, 1966.

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EXTERNAL RESPIRATION AND ACID-BASE BALANCE OF HUMAN BLOOD DURING LONG-TERM ANTIORTHOSTATIC HYPOKINESIA AND IN THE RECOVERY PERIOD

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[Article by A. P. Golikov, V. Ye. Vorob'yev, V. R. Abdrakhmanov, L. L. Stazhadze, V. V. Bogomolov and S. G. Voronina, submitted 3 Feb 78]

[English abstract from source]

The study of external respiration and acid-base equilibrium of blood of 35 test subjects exposed to 49-day head-down (—4°) tilting and of 6 test subjects exposed to 182-day head-down (—4) tilting demonstrated a trend for a decrease in the respiration rate, lung ventilation, oxygen consumption, and a relative increase in the exhalation time. With respect to the arterialized blood gases, a significant decrease in Pa_{O_2}, an increase in Pa_{CO_2} and in the O_2 alveolar-arterial difference were seen during the 49-day head-down tilting. During the 182-day head-down tilting a further increase in the CO_2 arterio-alveolar difference was noted. These changes suggest shifts of the ventilation-perfusion ration in the lungs and, probably, disturbances of central regulation of respiration induced by head-down tilting. During the recovery period the above changes diminished gradually and disappeared by the 14th and 30th day after the 49- and 182-day head-down tilting, respectively.

[Text] Studies have established that hypokinesia combined with antiorthostatic [head down] body position (simulation of one of the most important elements in the mechanism of effects of weightlessness on the body) induces changes in metabolic activity of tissues and gas exchange [1-5]. At the same time, the nature and severity of these deviations with increase in time of head-down position and hypokinesia have not been definitively determined.

Our objective here was to make a comprehensive study of external respiration and acid-base balance (ABB) of blood in a series of tests involving prolonged antiorthostatic hypokinesia (ANOH) and studies in the subsequent recovery period.

Methods

We studied external respiration and ABB in two series of studies involving 49- and 182-day ANOH (-4°).

In the first series with 49-day ANOH there were 35 essentially healthy males, ranging in age from 24 to 36 years. External respiration and blood ABB were examined at rest, in the morning of the background period (prior to ANOH), on the 30th and 49th days of ANOH, on the 1st, 7th and 14th days of the recovery period. No preventive measures were used during the period of ANOH, and such rehabilitation measures as therapeutic physical culture, massage, regulated motor activity and hydrotherapy were used in the recovery period.

Six essentially healthy men ranging in age from 33 to 39 years participated in the second series of studies; they were not submitted to any special preventive treatment during the 182-day period of ANOH. External respiration parameters and blood ABB at rest in the background period, on the 50th, 100th and 150th day of ANOH were used for analysis of the obtained data.

Lung volume was examined on a META-1-25B spirograph; gas composition of exhaled air was determined with a capnograph and paramagnetic oxygen analyzer. Oxygen uptake was calculated by the open system method. Ventilation parameters were adjusted to the BTPS system. ABB and gas composition of arterialized capillary blood were examined by the Astrup micromethod. The difference in CO_2 and O_2 tension for arterialized capillary blood and the last portion of exhaled air was considered as the respiratory gas gradient.

The results of the studies were submitted to statistical processing.

Results and Discussion

In the background studies, all of the parameters used were in the normal range (see Table). On the 30th day of ANOH we found slowing and reduction of minute volume of respiration, relative increase in expiration phase, decreased oxygen uptake and coefficient of oxygen utilization (CUO_2).

With reference to gas composition of alveolar air, there was a tendency toward decline of O_2 tension and reliable increase in CO_2 tension. Concurrently, a substantial decline of oxygen tension ($P<0.01$) and retention of carbon dioxide ($P<0.05$) were demonstrable in arterialized capillary blood. The arterioalveolar gradient for O_2 increased by a mean of 6 mm Hg. Against this background, several subjects presented deviations in rhythm of respiration.

In the first series of studies, by the end of the 49-day period of ANOH there was some tendency toward stabilization and even attenuation of the demonstrated deviations of gas exchange and metabolism, which is probably related to emotional factors due to nearing of the end of the ANOH period.

Dynamics of some parameters of external respiration and acid-base balance in the course of long-term ANOH (M±m)

Number of subjects	Time of exam.	RR	MV	exp/insp	$PACO_2$	PAO_2	$PaCO_2$	PaO_2	UO_2	CUO_2	pH	SB	BE
41	Background	12.2 0,39	7,9 0.28	1.1 0.03	39.4 0,27	98,8 0,64	39.7 0.22	89.9 0,89	3.7 0,20	40.2 1.38	7.390 0.008	23.9 0.14	—0.5 0,02
35	30 days ANOH	10.2 0.55	7.3 0.26	1.2 0.05	42.7* 0.84	97.5 0,68	42.9* 0.61	82.8** 1.09	3.1 0,31	33.4* 1,54	7.387 0,009	24.4 0.27	—0.5 0.03
41	49—50 days ANOH	10.6 0,48	7.5 0,22	1.4 0,05	40.8 0,35	96.9 0,73	40.9 0.62	86.3 1,05	3,5 0,41	37.5 1,26	7.390 0,010	23.1 0,20	—1.2 0,09
6	100 day ANOH	10.9 0.88	7.1 0.27	1.6 0.28	37.8 1.22	100,2 2,57	47.5* 2,45	85.3 3,07	3.2 0,19	36,0* 2.32	7.376 0,010	24.9 0.41	—0,7 0,44
6	150 days ANOH	9.7 0,79	7.8 0,19	1.4 0,28	36.7 2,10	99,7 2,25	44.8 3.19	82.7* 1.66	3,2 0,16	32.8* 2,07	7.385 0,010	24.7 0,56	—0.4 0,39

Key:

RR)	respiratory rate (per min)
MV)	minute volume (ℓ/min)
$PACO_2$, PAO_2)	CO_2 and O_2 tension in alveolar air (mm Hg)
$PaCO_2$, PaO_2)	CO_2 and O_2 tension in arterialized capillary blood (mm Hg)
exp/insp)	ratio of expiration phase to inspiration phase
UO_2)	oxygen uptake (mℓ/kg/min)
CUO_2)	coefficient of utilization of oxygen
SB)	standard bicarbonates (meq/ℓ)
BE)	base excess (meq/ℓ)

*Reliability of differences from background with $P<0.05$.
**Reliability of differences with $P<0.01$.

On the 100th and 150th days of ANOH, against the background of slower respiration and decline of O_2 tension in arterialized blood, there was a tendency toward decline of oxygen uptake and CUO_2), concurrently with increase in CO_2 tension. Analysis of alveolar air revealed worsening of conditions for exchange of gases, as manifested by decline of CO_2 tension, as compared to the 50th day of ANOH, with a tendency toward increase in O_2 tension. This was better demonstrable with retention of CO_2 in arterialized blood and further decline of blood O_2 tension. At this stage, there was an unbalanced exchange of gases, as indicated by the progressive increase in alveolar-arterial gradient and arteriolar-alveolar CO_2 gradient (Figure 1). While exchange of carbon dioxide (according to equilibrium of CO_2 tension in alveolar air and blood) was adequate and adjusted to new conditions in the period up to the 50th day of ANOH, when tested on the 100th and 150th days of ANOH there was a distinct tendency toward diminished efficiency of alveolar ventilation, as indicated by the significant difference in CO_2 tension in blood and alveolar air. Figure 2 illustrates the typical dynamics on the capnogram of subject P-v during prolonged ANOH. While there was close conformity of CO_2 in alveolar air and blood ($PACO_2$ 46.0 mm Hg, $PaCO_2$ 47.6 mm Hg) on the 50th day of ANOH, which was indicative of efficient exchange of gases for CO_2, with increase in duration of ANOH there was dissociation of CO_2 tension in blood and alveolar air ($PACO_2$ 40.6, $PACO_2$ 58.0 mm Hg on 100th day of ANOH; $PaCO_2$ 40.0 and $PaCO_2$ 53.0 mm Hg on the 150th day of ANOH), which was indicative of unbalanced exchange of gases.

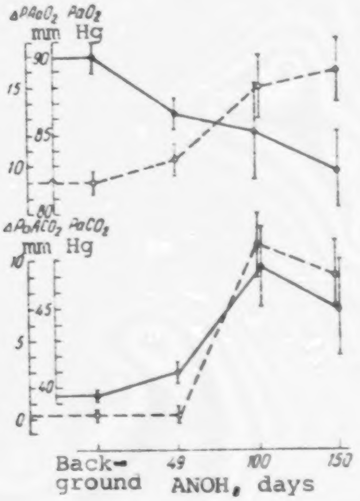

Figure 1.
Dynamics of O_2 and CO_2 tension in blood under the unfluence of ANOH

PaO_2, $PaCO_2$) O_2 and CO_2 tension in arterialized blood (solid lines)
$\Delta PAaO_2$) alveolar-arterial gradient for O_2
$\Delta PaACO_2$) arteriolar-alveolar gradient for CO_2 (dash line)

It should be noted that these changes in gas composition of blood were not associated with substantial shifts of pH, which is attributable, to some extent, to compensatory change in blood buffer systems and, in particular, retention of bicarbonates. We demonstrated a direct correlation between elevation of CO_2 tension in blood and compensatory retention of standard bicarbonates (coefficient of correlation +0.77). As maintained by L. L. Shik [6], an increase or decrease in pulmonary and alveolar ventilation, with unchanged level of metabolism, could be of adaptive significance under a number of conditions, and may be indicative of a capacity to control respiration in accordance with the needs of the body as an integral entity, even if this is related to deviations from stable $PACO_2$, rather than a flaw in respiratory regulation.

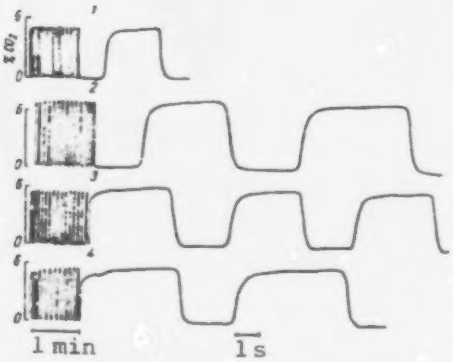

Figure 2.
Capnogram of subject P-v during ANOH with slow (25 mm/min) and rapid (750 mm/min) recording. Explained in the text.
1) background
2-4) 50, 100 and 150 days of ANOH

The deviations in gas exchange under the influence of prolonged ANOH are indicative of impaired ventilation-perfusion relations in the lungs. The gravitation factor has a substantial effect on the level of ventilation-perfusion relations, since the distribution of blood flow in the lungs changes substantially with change in body position [7]. Upon scrutinizing the genesis of disturbances in ventilation-perfusion relations under the influence of prolonged ANOH, we can detect an increase in specific weight of inadequately perfused alveoli (nonperfused component or alveolar gas shunt), as well as functional atelectases of part of the lung parenchyma (unventilated component or vascular alveolar shunt [8]). At the same time, we cannot rule out a decrease in alveolar-capillary diffusion of gases, particularly in cases of hemostasis in the lungs. However, in view of the high diffusion capacity of CO_2, it would be more correct to consider this a secondary mechanism in the genesis of deviations in gas exchange under the influence of prolonged ANOH.

It is also important to mention the fact that there was no correlation between minute ventilation and the main stimulus of respiration, CO_2 tension in blood (coefficient of correlation ranging from 0.162 to +0.134) on the 100th and 150th days of ANOH. This could be indicative of diminished sensitivity of the respiratory center to elevation of $PaCO_2$ or of other mechanisms of deviation of central regulation of respiration.

Thus, the observed deviations in exchange of gases under the influence of prolonged ANOH, being a special manifestation of functional adaptation to new living conditions, are apparently due to gravitational redistribution of body fluids [4], changes in central regulation of respiration and a change in conditions of pulmonary circulation [9], which leads to a change in ventilation-perfusion relations in the lungs and, perhaps, decline of their diffusion capacity. The maintenance of relatively stable ABB under these conditions is indicative of adequate compensatory and adaptive capabilities of the body with gradually developing changes in exchange of gases.

On the first day of the recovery period after 49-day ANOH with restriction of motor activity and orthostatic factors, the parameters of external respiration and ABB of blood did not demonstrate appreciable dynamics, with the exception of a tendency toward increase in respiration rate and ventilation indices. On the 7th day of rehabilitation, we observed a decline of O_2 and CO_2 tension in arterialized blood, against the background of lower CO_2 tension in alveolar air. With persisting tendency toward increase in gradient for O_2, the gradient for CO_2 was within the range of initial levels. At this time, the indices of O_2 uptake and CUO_2 remained low at rest, as compared to the background. Blood ABB at rest did not change appreciably. On the 14th day of the recovery period after 49-day ANOH, the indices of gas composition of blood and alveolar air were close to base levels.

It should be noted that physical loads at the early stage of the recovery period after 49-day ANOH were associated with strained respiration for the purpose of maintaining adequate exchange of gases, and this was manifested by an increase in ventilation indices with decline of blood O_2 and CO_2 tension, as well as appearance of blood ABB change in the direction of mixed acidosis. Thereafter, at the next stages of rehabilitation, physical loads induced a more adequate reaction with reference to blood ABB and external respiration.

At the early stage of the recovery period after 182-day ANOH, there were more marked disturbances referable to gas exchange and blood ABB, as manifested by low O_2 tension in arterialized blood (75.0±2.46 mm Hg), as well as changes in blood ABB in the direction of metabolic acidosis. The metabolic disorders were probably due to hemodynamic, circulatory disturbances at the early stage of readaptation. Under these conditions, we observed compensatory increase in pulmonary ventilation and increased CO_2 output ($PACO_2$ 45.5±1.37 mm Hg). The high gradient for O_2 (mean of 18.4 mm Hg) was also indicative of diminished efficiency of ventilation during this period. The demonstrated changes gradually regressed thereafter. However, low PaO_2 levels were observed up to the 14th day of the recovery period. The parameters of external respiration and blood ABB virtually failed to differ from base values on the 30th day after ANOH.

Thus, prolonged ANOH was associated with changes in external respiratory function. Extension of hypokinetic period led to deterioration of conditions for exchange of gases. The dynamics of the parameters studied in the recovery period were indicative of reversibility and functional nature of the deviations in gas exchange under the influence of prolonged ANOH.

BIBLIOGRAPHY

1. Kovalenko, Ye. A. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1977, pp 3-8.

2. Katkov, V. Ye.; Kauricheva, V. V.; Chestukhin, O. Kh.; et al. Ibid, No 5, pp 51-57.

3. Kotov, A. N. KOSMICHESKAYA BIOL., No 2, 1977, pp 85-86.

4. Belkaniya, G. S. Ibid, No 2, 1975, pp 3-8.

5. Fedorov, I. V., et al. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, Vol 2, 1975, pp 93-96.

6. Shik, L. L. in "Fiziologiya dykhaniya" [Physiology of Respiration], Leningrad, 1973, pp 44-62.

7. West, J. B. in "Advances in Respiratory Physiology," Baltimore, 1966, p 171.

8. Zil'ber, A. P. "Clinical Physiology for Anesthesiologists," Moscow, 1977, p 15.

9. Trushinskiy, Z. K.; Bogolyubov, V. M.; Anashkin, O. D.; et al. KARDIOLOGIYA [Cardiology], No 12, 1977, pp 90-94.

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DISTINCTIONS IN DEVELOPMENT OF PYROGENAL FEVER IN ANIMALS FOLLOWING PROLONGED HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 1, 1980 pp 46-50

[Article by P. V. Vasil'yev, G. D. Glod, S. I. Sytnik, N. N. Uglova and Y. P. Mel'nikova, submitted 22 May 78]

[English abstract from source]

The experiments on rabbits with pyrogenal fever and amidopyrine injection have demonstrated that their 15- and 30-day exposure to hypokinesia produces changes in the reactivity of thermoregulating centers, their overexcitation and depletion. These changes are more distinct after 15-day hypokinesia.

[Text] Concrete data must be obtained about the distinctions of development of pathological processes in order to deal with the practical aspects of the problem of developing methods of diagnostics and medical care of diseases occurring during space flights.

We have obtained some data on the effects of long-term restriction of movement on the course and development of inflammation [1] and hyperthermia.

In this work, our objective was to investigate the distinctions of development of experimental fever in hypokinetic animals. It is known that fever, like inflammation, is among the typical pathological processes associated with many diseases, and it reflects the state of reactivity of the body as a whole and thermoregulation in particular.

Methods

We used 48 male rabbits weighing 1.5-2 kg in our experiments. We produced 15- and 30-day hypokinesia by putting the rabbits in special cages [2]. Fever was induced immediately after removing the animals from the cages. Standard pyrogenal [purified protein-free pyrogenic of bacterial origin] from a culture of S. typhi was injected in the lateral vein of the ear, in a dosage of 1 MPD/kg. The state of heat regulation and sensitivity to pyrogenal were evaluated by the changes in rectal and ear temperature, heart and respiration rate. A copper-constantan thermocouple was used for thermometry with an accuracy of ±0.05°C. In addition, we used in some experiments the indices of the EKG, EMG of lumbar muscles and peripheral blood.

The obtained material was grouped and submitted to statistical processing.

Results and Discussion

The rabbits tolerated well the restricted mobility. The lag in weight gain constituted a mean of 129 and 171 g on the 15th and 30th day, respectively, of hypokinesia in control animals. The physiological parameters recorded at rest prior to inducing the fever did not differ appreciably from normal in experimental animals [Table 1).

Table 1. Physiological indices (M±m) of rabbits at rest prior to injection of pyrogenal

Group	Number of animals	Temperature, °C		Pulse rate, per min	Respiration, per min
		rectal	ear		
Control	13	38,7±0,16	27,9±0,5	239±7	132±17
15th day of hypokinesia	13	38,6±0,16	27,8±0,6	243±10	136±20
Control	11	38,9±0,15	27,3±0,9	233±7	127±17
30th day of hypokinesia	11	38,9±0,20	27,7±1,1	249±10	130±18

The pyrogenal injection induced the febrile reaction that is typical for a single injection of this product [3]. For the first 30 min after the injection, the majority of rabbits presented a 0.1-0.3°C drop of rectal temperature, after which heat began to accumulate in the body. The maximum elevation of temperature was the same in experimental and control animals constituting 1.2°C on the 15th day of hypokinesia and 1.3°C on the 30th day. However, the rate of development of hyperthermia varied. Thus, when inducing fever after 15 days of restricted movement the maximum temperature increment occurred on the average within 82±4 min and after 30 days of immobility, within 109±20 min. The fever developed more slowly in control animals, and the temperature peak occurred in the 151st±13 and 130th±19 min, respectively. The postpeak phase of the febrile cycle in experimental rabbits was characterized by a slower, sluggish course (Figure 1). The period of normalization of rectal temperature constituted a mean of 72.4 and 63.8% of total time of temperature reaction in experimental animals, versus 49.8 and 55.5% in the control.

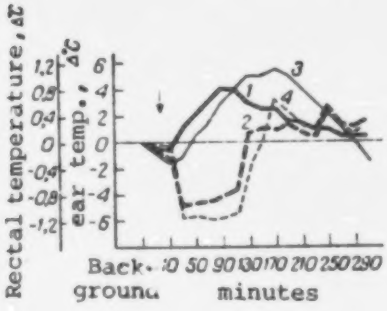

Figure 1.
Dynamics of temperature reaction of experimental (15th day of hypokinesia) and control rabbits during febrile period. Arrows point to time of pyrogenal injection

1, 2) change in rectal and ear temperature, respectively in experimental rabbit
3, 4) the same for control animal

The results of thermometry of the ear are of some interest, as they were indicative of the functional state of physical heat regulation in the rabbits. In the presence of fever on the 15th day of hypokinesia, maximum drop of ear temperature occurred simultaneously in both groups, reaching a mean of 3.7°C in the experimental group and 4.3°C in the control. On the 30th day, there was the same degree of decline (5.1°C) in ear temperature, but there was faster inclusion of physical heat regulation in the febrile reaction in control animals. It is remarkable that the interval between minimum ear temperature and maximum rectal temperature was almost 3 times shorter in experimental animals than controls on the 15th day of hypokinesia and 1.8 times shorter on the 30th day. The changeover to heat transfer by ear vessels during the febrile cycle after 2 weeks of hypokinesia also occurred much sooner (in the 59th min) than in the control. By the 30th day this difference diminished substantially.

In order to assess the functional coordination of different elements of thermoregulation, we analyzed the correlation between changes in rectal and ear temperature. The febrile cycle was arbitrarily broken down into three periods: elevation (first), stabilization (second) and restoration (third) of rectal temperature. Table 2 lists the results of processing the data.

Table 2. Coefficients of correlation between rectal and ear temperature of rabbits during fever

Period of fever	15-day hypokinesia	Control	30-day hypokinesia	Control
1	−0.9358	−0.7501	−0.9279	−0.8704
2	−0.3106	−0.8347	−0.2970	−0.3398
3	−0.6374	−0.7981	−0.4365	−0.8775

Analysis of these data indicates that there was a closer correlation between ear and rectal temperature during the period of temperature stabilization and restoration in control rabbits. In experimental animals, this function is less marked, which may be indicative of distinctive imbalance, of a change to another functional level of the mechanisms of heat regulation under the influence of hypokinesia.

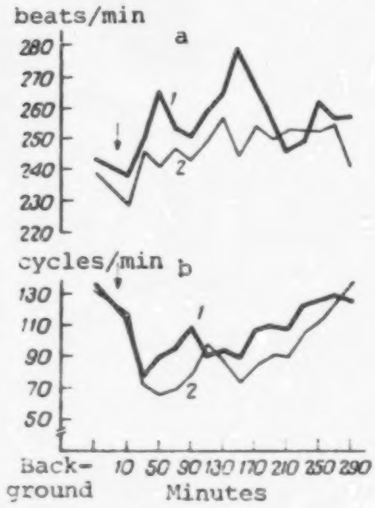

Figure 2.

Dynamics of pulse rate (a) and respiration (b) in rabbits during fever on 15th day of hypokinesia (mean data). Arrow indicates pyrogenal injection.
1) experimental rabbits
2) control animals

Analysis of the dynamics of heart and respiration rate (Figure 2), EKG and EMG during the access of fever led us to conclude that the prior hypokinesia had no appreciable effect on the above parameters. It should only be noted that the level of cardiac contractions and respiration during the fever was usually somewhat higher in experimental animals than the control, i.e., injection of pyrogenal induced greater strain on the cardiovascular system and less deviation of respiratory rate from the base level.

We know from the literature that heightened sensitivity to pyrogenal under the influence of any factors [4, 5] is usually associated with increased sensitivity of the heat-regulating center to antipyretics. In our experiments, hypodermic injection of amidopyrine in a dose of 100 mg/kg on the 15th and 30th days of restricted movement induced a substantial drop of body temperature (Figure 3). In experimental animals the maximum drop constituted a mean of 2.3°C and in controls 1.7°C, which could be indicative of heightened sensitivity of the former to antipyretics.

Thus, under the influence of prolonged restriction of movement, there is shortening of the phase of temperature elevation and extension of the postpeak period of experimental pyrogenal fever. After 15 days of hypokinesia, these distinctions in development of the access of fever were more marked than after 30 days. Consequently, certain changes in functional state of the heat-regulating center develop in the course of immobilization: increased reactivity at the early stages of fever, manifestation of torpidity and hyporeactivity of thermoregulation in the postpeak period of development of the process. There is impairment of coordination of function of different elements of this system, which apparently leads to attenuation and, perhaps, depletion of functional capabilities of the center for heat regulation. The change in reactivity to pyrogenal under the influence of hypokinesia was associated with increased sensitivity of the centers to antipyretics as well.

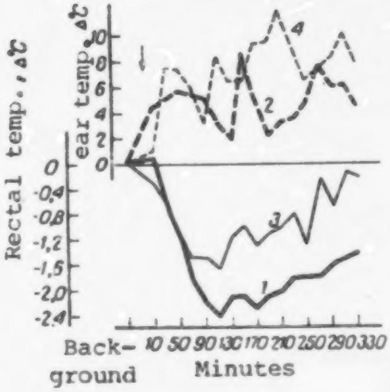

Figure 3.
Dynamics of temperature reaction of rabbits after injection of amidopyrine (15th day of hypokinesia). Arrow shows time of amidopyrine injection

1, 2) change in rectal and ear temperature of experimental rabbit
3, 4) same for control animal

The works of P. N. Veselkin et al. [3] have demonstrated convincingly that development and course of the febrile reaction are determined primarily by the functional state of the central nervous system, correlation between excitatory and inhibitory processes in its higher branches.

Yet it is known that hypokinesia worsens the functional state and adaptational capabilities of the central nervous system [5-7], and that inhibitory processes begin to predominate in the cerebral cortex [8-10].

In view of the foregoing, it may be assumed that, by virtue of the law of negative induction, there is "disinhibition" of subcortical vegetative centers, which cause increase in sensitivity of thermoregulatory systems, in the experimental rabbits. Moreover, under the influence of hypokinesia, the increased excitability is apparently combined with ready depletion of reactions, when maximum excitation of thermoregulatory centers is rapidly followed by inhibition thereof.

In spite of the dominant role of neural mechanisms in formation of the febrile reaction, disturbances in the endocrine system in the presence of hypokinesia [11-13] may also change appreciably the reactivity of the heat-regulating system and, consequently, the body's capacity to induce fever under new and unusual conditions [3, 14].

Further investigations will definitely be needed for deeper study of the pathogenesis of the effect of prolonged restriction of movement on development of fever.

BIBLIOGRAPHY

1. Vasil'yev, P. V.; Belay, V. Ye.; Gaydamakin, N. A.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1977, pp 41-46.
2. Savel'yev, T. P., and Krotov, V. P. Author Certificate 278291, USSR.
3. Veselkin, O. N. "Fever," Moscow, 1963.
4. Bystrova, L. N., and Kalinina, N. A. PAT. FIZIOL. [Pathological Physiology], No 3, 1973, pp 72-73.
5. Medvedeva, G. I. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 5, 1972, pp 750-753.
6. Krupina, T. N.; Vedorov, B. M.; Benevolenskaya, T. V.; et al. KOSMICHESKAYA BIOL., No 2, 1971, pp 76-81.
7. Ioffe, L. A. "Circulation and the Hypokinetic Syndrome," author abstract of doctoral dissertation, Moscow, 1971.
8. Kareva, T. A. in "Aktual'nyye voprosy kosmicheskoy biologii i meditsiny" [Pressing Problems of Space Biology and Medicine], Moscow, 1971, pp 129-131.
9. Khruleva, L. N. KOSMICHESKAYA BIOL., No 6, 1969, pp 75-78.
10. Reushkina, G. D. Ibid, No 2, pp 86-88.
11. Kalandarov, S. in "Gagarinskiye chteniya" [Gagarin Readings], Moscow, 1973, pp 191-200.
12. Fedorov, B. M., and Nevstruyeva, V. S. in "Predbolezn'" [Premorbid States], Moscow, Pt 2, 1969, pp 258-261.
13. Lazarev, N. V., and Grachev, A. M. in "Voyen.-med. akad. im. S. M. Kirova. Voyen.-nauch. o-vo slushateley. Itogovaya konf. Materialy" [Proceedings of Reporting Conference of the Military Scientific Society of Students, Military Medical Academy imeni S. M. Kirov], Leningrad, 1975, pp 105-106.
14. Gurgenashvili, N. I. PAT. FIZIOL., No 3, 1974, pp 67-69.

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RAPID LABORATORY METHOD FOR TESTING OUTGASING OF THERMOSTABLE PLASTICS AND RUBBER

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1980 pp 50-54

[Article by V. D. Yablochkin, G. D. Solomin, V. A. Shchirskaya, N. A. Glazkova, Ye. A. Demchenko, N. Ye. Ostasheva and E. I. Chukhno, submitted 23 Jan 78]

[English abstract from source]

Time-temperature dependence of concentrations of outgasing products of polymers and rubbers was studied. Applying the principle of time — temperature equilibrium, the exposure time for a laboratory rapid study of polymers at 100 °C was estimated to be 1 hr for enamels, lacquers and dyes, 1.5 hr for block and sheet polymers, 2.5 hr for sealants and rubbers, and 4 hr for textile materials, measured from the time when the preassigned temperature was achieved. The rapid method can be recommended for preliminary chemical study of polymers at the stage of their laboratory testing.

[Text] The migration of volatile substances in polymer materials and emission thereof into the environment is a diffusion process that is not governed by Fick's law [1], in which equalization of concentration of a substance that is nonuniformly distributed in the polymer follows the relaxation principle [2]. The previously expounded hypothesis [3] that relaxation of stresses in a polymer has an appreciable effect on the concentration of volatiles substances they emit subsequently gained experimental confirmation [4].

The study of relaxation processes in polymers made it possible to formulate the principle of equivalence or, as it is also called, temperature-time superposition [5], which means that the elevation of temperature affecting the polymer is equivalent to reduction of frequency of action of force or time of exposure to it. As shown by studies [6], relaxation time is exponentially related to temperature, while the logarithm of relaxation time is a linear function of absolute reciprocal temperature.

The principle of time-temperature equivalence, which has been used in a number of cases for accelerated studies of the process of "aging" of plastics [7], can apparently also be applied (in view of the similarity of various relaxation processes) for rapid study of gas emission by polymers. However, as it has validly been noted [7], experimental methods for accelerated "aging" cannot provide for complete reproduction of natural "aging" of plastics, and for this reason any express method can be recommended only for tentative evaluation of a group of similar materials in order to select the one with the best properties.

A previous study [8] demonstrated the possibility of using a rapid method for examining the products of outgasing of polymers used for ornamental and finishing purposes. Our main objective here was to develop a method for rapid examination of thermostable polymers and rubber used in construction.

Methods

This study involved the use of metal containers that could be sealed, 0.6 and 3.5 ℓ in size, equipped with sleeves and rubber thermostable membranes to collect air samples with a syringe. The containers were kept in an incubator, in which there was automatic regulation of temperature (with an accuracy of ±2°C) by means of electric heat through a water or air jacket. The temperature in the containers and incubator cabinets was measured and monitored by means of XA thermocouples connected to an EPP-09 potentiometer, and laboratory thermometers. We examined outgasing at temperatures of 40 to 100-120°C at 20°C intervals. At each temperature, we repeated the measurements every 30 min during an exposure period of up to 4 h (60-120 C) and every 1-3 days in the case of exposure for 10-15 days (in some cases up to 18-40 days; temperature of 40°C). We took 3-5 parallel readings at each point on the temperature curve.

We selected for our study 29 samples of thermostable polymers and (including four textile fabrics, nine enamels and varnishes, seven samples of plastics in blocks and sheets, five sealers and adhesives and 4 samples of rubber) manufactured on the basis of polysulfonimide, pyromellitimide, epoxy, melamine-formaldehyde and polyester resins, siloxanes and fluorine-containing elastomers. These materials contained organic solvents referable to the groups of alcohols, ketones, aliphatic and aromatic hydrocarbons, as well as esters, as volatile impurities. We used commercial samples that had been manufactured 3 months to 3 years prior to the study, containing different amounts of residual low molecular components.

In developing the conditions for rapid examination of polymer materials, we applied the principle of time-temperature equivalence, for which purpose we plotted summary graphs reflecting the concentration of products of outgasing as a function of exposure time at different temperatures, until they conformed with the selected equilibrated level.

This procedure enabled us to evaluate the entire range of exposures at the selected temperature. In this regard, previously described methods of gas chromatography [3] were used to analyze the qualitative and quantitative composition of the products of outgasing of thermostable polymers and rubber at standard saturation (1 kg/m^3 or 1 m^2/m^3). The objective was to choose optimum temperatures and exposure times, with which the qualitative and quantitative composition of outgasing would not differ appreciably from the composition of equilibrated concentrations at a temperature of 40°C.

Results and Discussion

It was established that there is an increase in concentration of volatile substances with increase in temperature and exposure, and the nature of outgassing is graphically described by a linear or exponential function (Figures 1-4). At a temperature of 60°C and exposure time of 4 h, the concentrations of volatile substances did not usually reach the equilibrated levels obtained at 40°C (exposure time 10-15 days), while at 120°C the initial concentration of volatile substances after exposure for 30 min was considerably higher than the equilibrated. Such patterns were noted when we tested polymers referable to most of the groups studied; for this reason, although the products of thermal oxidative destruction could not be demonstrated, even with the top temperature of 120°C, we could only select the range of 80-100°C for rapid testing of most of the materials. However, at a temperature of 80°C, exposure of the samples to "sealing" constituted more than 4 h in many cases, therefore a temperature of 100°C was the most common and convenient condition for testing materials from different groups.

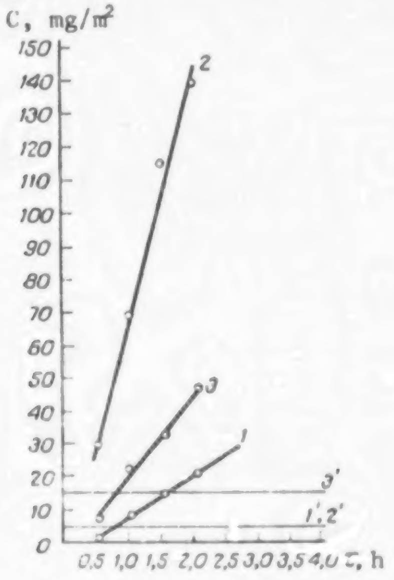

Figure 1.
Concentration of volatile substances emitted by enamel based on epoxy resin as a function of exposure time

1, 2) butylacetate (100 and 120°C, respectively
3) ethylbenzene (100°C)
1'-3') respective levels of equilibrated concentration at 40°C

Exposure time was chosen in the time interval of 40 min to 4 h, and it was defined as the result of intersection of the curves of outgasing at 100°C on the curve of concentration of volatile products as a function of exposure time [to sealing] with a base line corresponding to an equilibrated level of concentrations of the component in question at a temperature of 40°C, which was usually established in the sealed containers on the 7th-15th day.

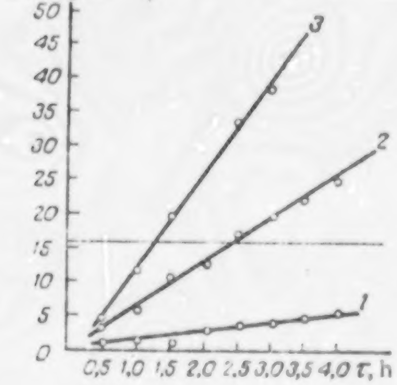

Figure 2.
Concentration of acetone discharged from carbon-containing plastic as a function of exposure time
1-3) 60, 80 and 100°C temperatures, respectively
Dash line refers to level of equilibrated concentration at 40°C

Figures 1-4 illustrate the results of studying outgasing of some materials as a function of their exposure to sealing. As can be seen from the submitted data, the time the outgasing curves reach an equilibrated level is related not only to the type or group to which a material belongs, but chemistry of the vovolatile component, and it is the latter circumstance that presented difficulties in selecting the exposure time for rapid testing of materials in different groups. Evidently, under such conditions, one could only choose some average or maximum exposure time, with due consideration of possible variations in chemical composition of the complex of products of outgasing from polymers in a given group. Evidently, the differences in time of attainment of an equilibrated level could be attributed to the distinctions in diffusion of chemicals in the materials and their quantitative content in the tested samples. Model samples of polymers and rubber with a specific amount of volatile impurities (0.25 to 1%) were prepared for experimental verification of the distinctive features of the effect. As a result, it was established that there was no appreciable difference in time of attainment of equilibrated level with increase to 1% in styrene content in a rubber sample based on butadiene-styrene rubber at 100°C. The same was observed in the case of rubber based on fluorine-containing elastic (see Figure 3) at temperatures of 80 and 100°C, with 0.5 to 1% hexane content; however, in the range of 0.25 to 0.5% at a temperature of 100°C, we observed some increase in exposure. It should be noted that the concentration factor was very important in the case of low levels of volatile products in the material. Thus, sealing time constituted up to 4 h for fabrics containing trace amounts of volatile products, whereas for enamels, where the residual level of volatile substances reached several percentage points, it did not exceed 1 h.

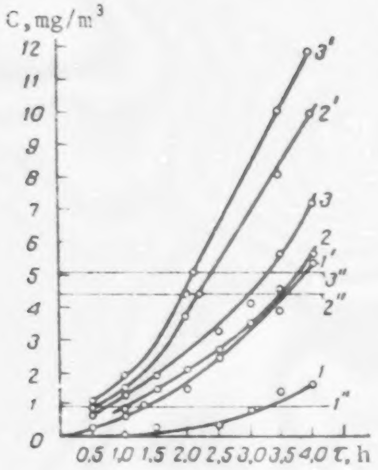

Figure 3.
Concentration of n-hexane discharged by samples of rubber based on fluorine-containing elastic containing different amounts of volatile components as a function of exposure to sealing

1, 1') 0.25% concentration at 80 and 100°C, respectively
2, 2') 0.5% concentration at 80 and 100°C
3, 3') 1% concentration at 80 and 100°C
1"-3") corresponding levels of equilibrated concentration at 40°C

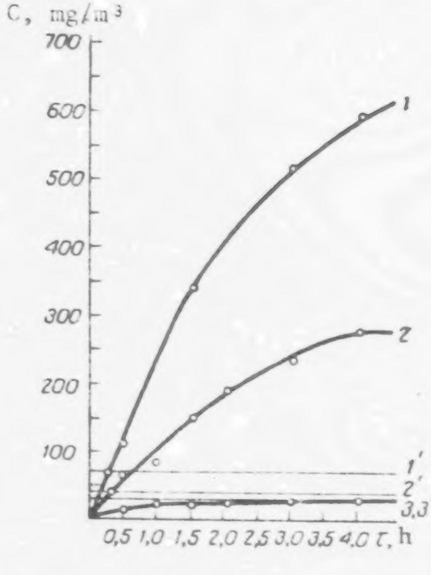

Figure 4.
Concentration of volatile substances discharged by plexiglas based on polymethyl methacrylate (at 100°C) as a function of exposure of sample to sealing

1) methanol ($D = 0.24 \cdot 10^{-9}$ cm²/s)
2) ethanol ($D = 0.24 \cdot 10^{-9}$ cm²/s)
3) benzene ($D = 5.50 \cdot 10^{-9}$ cm²/s)
1'-3') corresponding levels of equilibrated concentration at 40°C temperature

Another factor that has some influence on exposure time is the rate of diffusion of substances in the material, which is determined by coefficients of diffusion that have been studied experimentally for a small number of chemicals as related to widely used polymers. We tracked the significance of this factor on the example of a model sample of plexiglas based on polymethyl methacrylate containing as impurities methanol, ethanol and benzene, for which the values of coefficients of diffusion are known [9]. As can be seen from the curves illustrated in Figure 4, the time of attainment of an equilibrated level constituted 15-20 min for methanol and ethanol (coefficient of diffusion $D = 0.24 \cdot 10^{-9}$ cm^2/s) and 4 h for benzene ($D = 5.5 \cdot 10^{-9}$ cm^2/s); for this reason the chioce of exposure time for rapid testing of this material could be made only on the basis of calculation of the mean time of attainment of equilibrated levels of components of outgasing inherent in a given sample. Calculation of mean sealing exposure times for materials referable to different groups yielded the following values (in min): 225±15 for fabric, 49±15 for enamels and other varnishes, 84±15 for block and sheet plastics, 85±50 for adhesives and sealers, 109±41 for rubber.

Thus, the rapid testing of thermostable polymers and rubber can be done at a temperature of 100°C and exposure time of 1 to 4 h for different groups, which reduces significantly the time required for laboratory testing, which is currently performed at a temperature of 40°C and requires 10-15 days. Exposure time should be counted from the moment a specified temperature has been reached for the material, while the concentration of volatile substances formed in the gas environment and demonstrated at that time should be considered as background and deducted from the final results. It is quite obvious that this procedure implies the use of high-speed instrumentation for analysis, which is highly sensitive and specific and does not require large volumes of air for the analyses. When running rapid tests, the choice of other experimental parameters (temperature and exposure time) can be made on the basis of the logarithm of exposure time of a sample as a graphic function of the reciprocal of absolute temperature, which is linear, as was shown by the results of experiments with various materials.

In conclusion, it should be noted that the findings from testing samples of materials referable to each of the groups do not serve as sufficient grounds to derive a categorical conclusion concerning the time required for rapid ["express"] testing thereof. For this reason, as experimental data are accumulated in the course of work dealing with sanitary and chemical testing of new polymers, there may be some adjustment and further definition of exposure time [for sealing] for materials referable to different groups.

BIBLIOGRAPHY

1. Reytlinger, S. A. "Permeability of Polymers," Moscow, 1974.

2. Vasenin, R. M., and Chernova, I. V. VYSOKOMOLEKULYARNYYE SOYEDINENIYA [High Molecular Compounds], No 11, 1966, pp 2006-2011.

3. Jablochkin, V. D., et al. REV. MED. AERONAUT., Vol 12, 1973, pp 305-308.

4. Khofbauer, E. I.; Bebchuk, T. S.; et al. ZH. PRIKLADN. KHIMII [Journal of Applied Chemistry], No 2, 1976, pp 391-396.

5. Aleksandrov, A. P., and Lazurkin, Yu. S. ZH. TEKHN. FIZIKI [Journal of Industrial Physics], Vol 9, 1939, p 1249.

6. Lazurkin, Yu. S. Ibid, pp 1261-1266.

7. Pavlov, N. N. in "Pererabotka plasticheskikh mass" [Processing of Plastics], Moscow, 1966, pp 249-253.

8. Demchenko, Ye. A.; Glazkova, N. A.; Chukhno, E. I.; et al. in "Aktual'nyye problemy kosmicheskoy biologii i meditsiny" [Pressing Problems of Space Biology and Medicine], Moscow, Vol 1, 1977, pp 8-9.

9. Zhurkov, S. N., and Ryskin, G. Ya. ZH. TEKHN. FIZIKI, Vol 24, 1954, pp 797-810.

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EFFECTS OF 25 AND 50 MeV PROTONS ON HUMAN PERIPHERAL BLOOD LYMPHOCYTE CHROMOSOMES IN VITRO

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1980 pp 54-60

[Article by A, M. Totseva, N. I. Ryzhov, V. N. Gerasimenko and Ye. Dermendzhiyev, submitted 21 Feb 78]

[English abstract from source]

The frequency and type of chromosomal abberations in human lymphocytes induced by 25, 50, 645 MeV protons and 200 kv x-rays were studied. It was shown that the yield of one-hit acentric fragments increased linearly and that of double-break aberrations increased exponentially with the irradiation dose. It was demonstrated that under the influence of radiations with high linear energy transfer the number of paired fragments increased and that of dicentrics and rings decreased. The test of total yield of chromosomal aberrations and their specific types helped to derive coefficients of relative biological effectiveness of the above irradiations. There was a quantitative correlation between the dose and yield of individual aberration types. This suggests that lymphocytes can be used as a biological dosimeter for dose measurement.

[Text] In our preceding report [1] we submitted the results of a study of radiation damage to the chromosome system of human lymphocytes under the influence of 645 MeV protons. We demonstrated the nature and main parameters of yield of different types of chromosomal aberrations as a function of dosage. It was shown that the coefficients of relative biological effectiveness (RBE) are close to 1 for protons, according to incidence of single and double breaks, as well as total yield of aberrations. The fact that these studies were conducted on human lymphocytes and that there was a clearcut quantitative identity of effects of in vitro and in vivo irradiation of lymphocytes enabled us to extrapolate, with a high degree of reliability, the data obtained for the RBE of 645 MeV protons to the integral human body, and to use them to set standards for radiation exposure during space flights [2].

The presence of protons with lower energy in space radiations served as the grounds to continue these studies in order to obtain information about the biological effects of such radiation on the chromosome system of human lymphocytes.

In this work, we analyzed the results of studies involving exposure in vitro of cultures of human lymphocytes from peripheral blood to 25 and 50 MeV protons. Some of the preliminary results of the studies were reported in previously published works [3, 4].

Methods

Lymphocytes from human peripheral blood were cultured by the method of Moorhead et al. [5] with some modifications [6]. The cultures were exposed to radiation in doses of 25, 50, 100, 200 and 400 rad 3-6 h after addition of phytohemagglutinin. X-rays were delivered at 200 kV, 15 mA and dose rate of 0.95 rad/s. The synchrocyclotron of the Joint Institute of Nuclear Research (Dubna) was used to deliver protons. The dose rate of 50 and 25 MeV protons constituted 0.40 and 0.35 rad/s, respectively. Culturing lasted 2 days at 37°C. The cultures were treated with colchicine in a concentration of 5 μg/m after 48 h and they were fixed 3 h later. The preparations were stained according to Giemsa.

We selected for analysis metaphase plates with well-dispersed chromosomes. We analyzed the quantitative chromosomal changes and structural aberrations of chromosomes. Chromatid and paired acentric fragments were classified as single-hit aberrations, while double-hit ones included dicentrics and rings with one paired fragment, interstitial deletions and translocations [7]. Genes were not taken into consideration in the analysis.

Results and Discussion

The results of our study of radiation-induced genome mutations revealed that the yield of aneuploid cells depended little on dosage and did not substantially exceed 10% of the cells examined (Table 1), within the error margin of the experiment, under the influence of all tested levels of proton energy. It is believed [8, 2] that the presence of such cells in the first mitosis is related primarily to the technique used to make the preparations. We believe that one should also not rule out the possibility of induction of aneuploid cells as a result of the effect of radiation. We base this conviction on the presence of a tendency common to proton of all tested energy levels toward approximately twofold increase in yield of cells with altered chromosome number (referable to polyploidy and endoreplication) with increase in dosage from 25 to 400 rad (Figure 1).

Table 2 lists the results of the study of chromosomal aberrations of different types and forms thereof as a function of dosage of radiation and energy of protons. For the sake of comparison, data are given on structural chromosomal aberrations of lymphocytes when exposed to 645 MeV protons and x-rays. We must call attention to the low yield of chromatic aberrations, as well as the fact that it is independent of radiation dose, proton energy or type of radiation.

Table 1. Quantitative chromosomal changes

Type of radiation	Dose, rad	Poly-ploidy, %	Endo-replica-tion, %	Total aneuploid cells, %
X-rays	Control	—	—	0,3
Protons, MeV:				
645		—	—	—
50		—	—	0,5
25		—	—	—
X-rays		—	—	1,0
Protons, MeV:				
645		—	—	3,0
50	25	2,0	0,5	4,5
25		—	—	0,5
X-rays		—	—	0,5
Protons, MeV:				
645		—	0,5	5,0
50	50	1,0	—	4,5
25		—	—	2,5
X-rays		—	—	1,5
Protons, MeV:				
645		—	—	4,0
50	100	—	1,0	5,0
25		—	0,5	3,5
X-rays		—	—	2,0
Protons, MeV:				
645		1,5	—	7,5
50	200	1,0	1,5	6,0
25		1,0	—	7,0
X-rays		1,0	—	4,5
Protons, MeV:				
645		2,0	—	6,0
50	400	5,0	2,0	10,5
25		4,0	2,0	10,0

The yield of paired acentric fragments as a function of radiation dosage is clearly linear (Figure 2), for both the three energies of protons and x-rays. Data processing by the least squares method revealed that the dose-effect function for paired fragments is well approximated by the equation $Y = \alpha D^{n}$, where Y is the yield of paired fragments (%), D is the radiation dose (rad), α is the coefficient of proportionality and n is the hit index. For paired acentric fragments, we obtained the following equations:

$$Y_{25\ \mathrm{MeV}} = 2{,}08 \cdot 10^{-3} \cdot D^{(0{,}98 \pm 0{,}09)}, \qquad (1)$$

$$Y_{50\ \mathrm{MeV}} = 1{,}42 \cdot 10^{-3} \cdot D^{(1{,}03 \pm 0{,}09)}, \qquad (2)$$

$$Y_{645\ \mathrm{MeV}} = 0{,}93 \cdot 10^{-3} \cdot D^{(1{,}06 \pm 0{,}22)}, \qquad (3)$$

$$Y_{\mathrm{roentgen}} = 0{,}68 \cdot 10^{-3} \cdot D^{(1{,}06 \pm 0{,}11)}. \qquad (4)$$

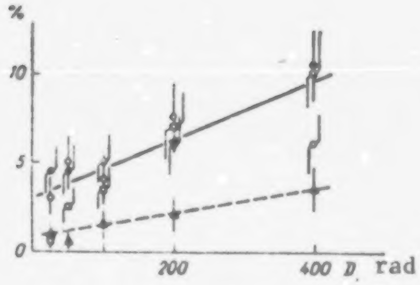

Figure 1.
Yield of aneuploid cells as a function of radiation dose. Here and in Figures 2 and 3: triangles--x-rays; squares--protons with energy of 25 MeV; black and white circles--protons with energy of 50 and 645 MeV, respectively

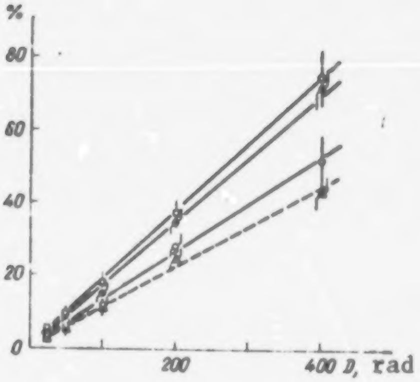

Figure 2.
Yield of paired acentric fragments as a function of radiation dose

We can interpret the linear correlation between yield of paired acentric fragments (single-hit breaks) and radiation dosage on the basis of the classical conceptions of quantitative radiobiology [9]. A comparison of equations (1-3) also indicates that there is an increase in yield of single-hit aberrations with decline of proton energy. It is quite difficult to provide a satisfactory explanation for this effect, in view of the significant complexity of the intimate mechanism of development of chromosomal damage. Evidently, the increase in proton-proton interaction and in linear energy transfer (LET) are responsible for the demonstrated changes in yield of single-hit aberrations. The significance of LET of radiation in induction of the above aberrations has been discussed rather comprehensively in previously published works [10, 11].

Figure 3 illustrates the dose functions referable to double-hit chromosomal aberrations for x-rays and protons differing in energy. We determined the overall yield of dicentrics and rings. The yield thereof as a function of dosage of radiation for protons and x-rays can be described by the following equations:

$$Y_{25\ \mathrm{MeV}} = 1.01 \cdot 10^{-4} \cdot D^{(1.35 \pm 0.16)}, \tag{5}$$

$$Y_{50\ \mathrm{MeV}} = 1.53 \cdot 10^{-4} \cdot D^{(1.34 \pm 0.14)}, \tag{6}$$

$$Y_{645\ \mathrm{MeV}} = 1.80 \cdot 10^{-4} \cdot D^{(1.40 \pm 0.11)}, \tag{7}$$

$$Y_{\mathrm{roentgen}} = 0.98 \cdot 10^{-4} \cdot D^{(1.50 \pm 0.10)}. \tag{8}$$

Table 2. Incidence of chromosomal aberrations

Type of radiation	Dose, rad	Cells counted	Type of chromosomal aberrations: chromatid breaks, %	chromosome breaks, %	interstit. deletions, %	dicentrics, %	tricentrics, %	rings, %	interchromosome exchanges, %	Cells with aberrations %	Total aberrations, %	Total breaks, %
X-rays	0	300	2,3	—	—	—	—	—	—	2,3	2,3	2.3
Protons, MeV:												
645		200	3	—	—	—	—	—	—	3	3	3
50		200	2	—	—	—	—	—	—	2	2	2
25		200	2	—	—	—	—	—	—	2	2	2
X-rays	25	200	2,5	2,5	—	1	—	1	—	7	7	9
Protons, MeV:												
645		200	3	3	—	2	—	—	—	7,5	8	10
50		200	2,5	4,5	—	2	—	—	—	8	9	11
25		200	3	5,5	0,5	0,5	—	—	—	8	9,5	10,5
X-rays	50	200	2	5	1	4	—	—	—	9	12	17
Protons, MeV:												
645		200	2	5,5	0,5	4,5	—	0,5	—	11,5	13	18,5
50		200	4	9	—	3,5	—	0,5	—	13	17	21
25		200	2	9,5	0,5	2	—	0,5	—	12,5	14,5	17,5
X-rays	100	260	2.7	12	1,5	7,3	—	1,5	0,7	23	25.7	36.7
Protons, MeV:												
645		200	3	11,5	2,5	9	—	1	1	25	28	41,5
50		200	1	15	1	7	—	—	0,5	17,5	24,5	33
25		200	2,5	18	1	6	—	—	0,5	24	28	35,5
X-rays	200	200	3.5	24	7,5	25	—	3	1,5	48	64,5	101,5
Protons, MeV:												
645		500	2.6	29.4	7,5	31	—	2,5	1	52	73,5	115,5
50		200	2,5	34	2,5	14	—	2	1	30,5	56	75,5
25		200	5	37	2	10,5	—	2,5	1	46,5	58	74
X-rays	400	200	4	42,5	15	66	1,5	14	3,5	79	146,5	249,5
Protons, MeV:												
645		100	2	51	20	69	2	14	1	84	159	269
50		200	3	71	7	45	—	6	3	68	135	196
25		100	4	74	8	30	—	4	2	80	122	166

Analysis of equations (5-7) shows that there is a decline in yield of dicentrics and rings with increase in LET. The overt nonlinear nature of yield of aberrations as a function of dosage and obtained values of $n<2$ are consistent with the data of other authors [12, 13]. Since intra- and inter-chromosomal exchanges are double-hit aberrations, one should have expected the correlation to dosage to be quadratic in equations (5-8). However, in view of the fact that a certain share of the exchanges occurs in the presence of two injuries induced by passage of one particle [9], as well as the result of postradiation repair of some chromosomal lesions [14], there occurred the deviation that we observed in n from 2 in the direction of a decline. As to the correlation we observed in the experiment between overall yield of dicentrics and rings, on the one hand, and proton energy, on the other, we can concur with the authors [9, 15] who assume that the yield of interchromosomal exchanges depends on the mean distance between rather closely situated segments of chromosomes which, in turn, is determined by the range and LET of protons, and secondary ionizing particles. We cannot rule out the possibility that there is also a change in nature of damage to chromosomes with decrease in proton energy, as a result of which the probability of expression of exchanges diminishes.

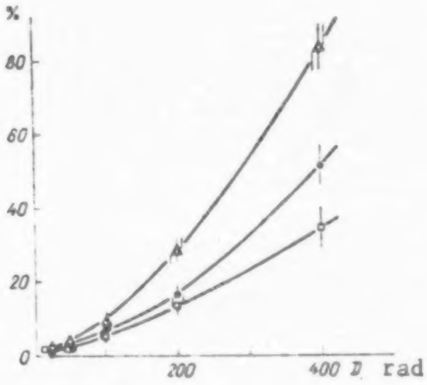

Figure 3.
Overall yield of dicentrics and rings as a function of radiation dosage

As previously indicated, the sensitivity of chromosomes to radiation, prolonged retention of cytogenetic effects, approximately the same quantitative and qualitative effects of in vitro and in vivo irradiation of human lymphocytes, as well as a number of other factors, have resulted in using human lymphocytes as a "biological dosimeter." Dose-effect functions were obtained for different types of ionizing radiation over a wide range of doses and energies, and they make it possible to define the radiation dose and, accordingly, severity of radiation lesion to man according to yield of chromosomal aberrations of different types types with the degree of accuracy that is required for practical purposes. There are different opinions as to the type of chromosomal aberration that should be used to determine the radiation dose. In essence, these are single-hit aberrations, dicentrics and rings, the yield of aberrant cells, total number of aberrations and number of aberrations per aberrant cell [16-18]. Evidently, one of the most important criteria for assessing the severity of radiation damage is the total yield of chromosomal aberrations. According to the results of our experiments, parameters of the dose function for this criterion were obtained, and they are represented in the following equations:

$$Y_{25\ \mathrm{MeV}} = 2.89\cdot 10^{-3}\cdot D^{(0.94\pm 0.09)}, \tag{9}$$

$$Y_{50\ \mathrm{MeV}} = 2.20\cdot 10^{-3}\cdot D^{(1.00\pm 0.10)}, \tag{10}$$

$$Y_{645\ \mathrm{MeV}} = 1.90\cdot 10^{-3}\cdot D^{(1.02\pm 0.10)}, \tag{11}$$

$$Y_{\mathrm{roentgen}} = 1.70\cdot 10^{-3}\cdot D^{(1.02\pm 0.08)}. \tag{12}$$

Analysis of these data demonstrates the significant resemblance of the dose function, in essence for all radiations studied, the great closeness to 1 of the values of "hit" coefficients, and this enables us to use the equations for determination of dosage according to magnitude of the biological effect. At the same time, it should be noted that the significant concentration of initial segments of the dose curves together, corresponding to the effects of relatively low doses of radiation, will most probably contribute substantial difficulties in identifying the type and energy of radiation. However, in the case of high doses, identification of proton energy could be made easier with availability of information about the ratio of single-hit aberrations to double-hit ones, which differ significantly in the range of tested proton energy.

Table 3. RBE coefficients for 25, 50 and 645 MeV protons

Proton energy, MeV	RBE coefficient		
	paired fragments	dicentrics and rings	total aberrations
645	1,10±0,09	1,0±0,09	1.08±0,03
50	1.40±0,10	0,6±0,40	0,98±0,07
25	1.50±0,11	0.5±0,30	1,00±0,09

Equations (9-12) also make it possible to obtain the RBE coefficients for 25, 50 and 645 MeV protons. In principle, equations (1-8) can also be used for this purpose. However, analysis of the data in Table 2, Figures 2 and 3 indicates that the RBE coefficients for 25 and 50 MeV protons are different for different chromosomal aberrations; moreover, the values of RBE are also different in different doses ranges for dicentrics and rings, the yield of which is a nonlinear function of dosage (Table 3). For this reason, it is preferable to use the data on total yield of aberrations in order to determine the RBE for 50 and 25 MeV protons. According to this criterion, the RBE for 25 and 50 MeV protons constituted 1.0±0.1 and 0.98±0.07, respectively.

Thus, our studies revealed that exposure of human lymphocytes to 25, 50 and 645 MeV protons in vitro induces various types of chromosomal aberrations in them. In all cases, we observed a linear increase in single-hit and gradual increase in multihit aberrations with increase in dosage. It was also shown that there is an increase in paired fragments, as well as a decrease in yield of dicentrics and rings, under the influence of radiation with high LET. There was a quantitative correlation between dosage and overall yield of aberrations, which suggests that lymphocytes could be used as a biological dosimeter for determination of dosage. The RBE coefficients for 25 and 50 MeV protons were determined from the criterion of total yield of aberrations, and they were found to equal 1.

BIBLIOGRAPHY

1. Ryzhov, N. I., et al. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1973, pp 79-83.

2. Bochkov, N. P. "Human Chromosomes and Radiation," Moscow, 1971.

3. Totseva, A. M. in "Bolgarskaya natsional'naya konf. po med. genetike i biologii" [National Bulgarian Conference on Medical Genetics and Biology], Varna, 1972, p 55.

4. Idem, "First Worldwide AMIE Congress," Varna, 1972, p 167.

5. Moorhead, P. S., et al. EXP. CELL. RES., Vol 20, 1960, pp 613-618.

6. Gol'dman, I. L., and Levina, L. Ya. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 11, 1964, pp 103-107.

7. Bochkov, N. P., et al. GENETIKA [Genetics], No 5, 1972, pp 133-141.

8. Antoshchina, M. M. RADIOBIOLOGIYA [Radiobiology], No 1, 1968, pp 89-91.

9. Li, D. Ye. "Effect of Radiation on Living Cells," Moscow, 1963.

10. Sevan'kayev, A. V., et al. in "Radiatsiya i organizm" [Radiation and the Organism], Obninsk, 1975, pp 93-94.

11. Lloyd, D. C., et al. INT. J. RADIAT. BIOL., Vol 28, 1975, pp 75-90.

12. Sevan'kayev, A. V., and Bochkov, N. P. GENETIKA, No 5, 1968, pp 130-137.

13. Todorov, S., et al. MUTAT. RES., Vol 15, 1972, p 215.

14. Dubinin, N. P., and Tarasov, V. A. in "Sovremennyye problemy radiatsionnoy genetiki" [Current Problems of Radiation Genetics], Moscow, 1969, pp 7-78.

15. Wolff, S., et al. J. BIOPHYS. BIOCHEM. CYTOL., Vol 4, 1958, pp 368-374.

16. Bender, M. A., and Gooch, P. C. RADIAT. RES., Vol 29, 1966, pp 568-582.

17. Norman, A. in "Human Radiation Cytogenetics," Amsterdam, 1967, p 53.

18. Sasaki, M. S., and Miyata, H. NATURE, Vol 220, 1968, pp 1189-1193.

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DEVELOPMENT OF PROGRAM FOR THE CONTROL OF THE AUTOTROPHIC COMPONENT OF AN ECOLOGICAL SYSTEM THAT IS CLOSED WITH REGARD TO EXCHANGE OF GASES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1980 pp 60-63

[Article by A. S. Nasonov and V. S. Toroptsov, submitted 3 May 77]

[English abstract from source]

The requirements for the programmed control and performance of autotrophic and heterotrophic components of a closed ecological system were determined. Stability of the system can be assured, if these requirements are met. The paper gives examples of pertinent computations.

[Text] This work completes the study of programmed control of the autotrophic element, which we began previously [1]. We have defined the set of requirements that must be imposed on the parameters of programmed control and productivity of components in order to create a system that would be stable in exchange of gases.

Definition of the Control Program

In order to define the control program within the range of a specified cycle for system operation, $T_C = \tau_1 + \tau_2$, let us estimate the time τ_1 and τ_2 of operation of the autotrophic component in each of modes I_1 and I_2.

From system (2) [1], with consideration of the expressions for mean volumetric rates of oxygen output and carbon dioxide uptake by the autotrophic component in time T_C, we obtain:

$$\tau_2 = \frac{V_x^{01}(\bar{y}) \cdot \sum_{i=1}^{n} V_{y_i} - V_y^{01}(\bar{y}) \cdot \sum_{i=1}^{n} \overline{V}_{x_i}}{V_x^{01}(\bar{y}) \cdot V_y^{02}(\bar{y}) - V_y^{01}(\bar{y}) \cdot V_x^{02}(\bar{y})}; \qquad (1)$$

$$\tau_1 = T_C - \tau_2. \qquad (2)$$

In view of the fact that $0 \leqslant \tau_2 \leqslant T_C$, we shall have:

$$0 \leqslant \frac{V_x^{01}(\bar{y}) \cdot \sum_{i=1}^{n} V_{y_i} - V_y^{01}(y) \cdot \sum_{i=1}^{n} V_{x_i}}{V_x^{01}(\bar{y}) \cdot V_y^{02}(y) - V_y^{01}(\bar{y}) \cdot V_x^{02}(\bar{y})} \leqslant 1, \tag{3}$$

which can be transformed to the following appearance:

$$0 \leqslant \gamma = \frac{\sum_{i=1}^{n} V_{x_i} \cdot (R_\Gamma - r^{01})}{V_x^{02}(\bar{y}) \cdot (r^{02} - r^{01})} \leqslant 1, \tag{4}$$

where γ is the share of autotrophic element operating time in mode I_2, within the range of the set cycle, and R_Γ is the coefficient of respiration of the sum of heterotrophic components:

$$\left(R_\Gamma = \frac{\sum_{i=1}^{n} V_{y_i}}{\sum_{i=1}^{n} V_{x_i}} \right);$$

r^{01}--photosynthetic coefficient of autotrophic component in mode I_1

$$\left(r^{01} = \frac{V_y^{01}(\bar{y})}{V_x^{01}(\bar{y})} \right);$$

r^{02}--photosynthetic coefficient of autotrophic component in mode I_2

$$\left(r^{02} = \frac{V_y^{02}(\bar{y})}{V_x^{02}(\bar{y})} \right.$$

The share of operating time for the autotrophic component in mode I_1, within the range of the set cycle is $\beta = 1 - \gamma$.

Thus, equation (4) is a mandatory and sufficient condition for creating a stable system, closed for gas exchange, for two modes of operation.

The above proof of stability will also be valid for the case when the second mode I_2 is referable to darkness:

$$V_x^{02}(\bar{y}) = V_x^{02} = \text{const} < 0 \text{ и } V_y^{02}(\bar{y}) = V_y^{02} = \text{const} < 0.$$

In this case, condition (4) can be written down in the following form:

$$0 \geqslant \frac{R_r - r^{01}}{r^{02} - r^{01}} \geqslant \frac{V_x^{02}}{\sum_{i=1}^{n} V_{x_i}}.$$

In this case, if functions $V_y^{01}(\bar{y})$ & $V_x^{01}(\bar{y})$ are submitted in the following form [2]:

$$V_y^{01}(\bar{y}) = V_y^{01}(\bar{y} - A);$$

$$V_x^{01}(\bar{y}) = \frac{V_y^{01}}{r^{01}} \cdot (\bar{y} - A) = V_x^{01} \cdot (\bar{y} - A),$$

where $V_y^{01} > 0$, $V_x^{01} > 0$ & $A > 0$, the operating time of the autotrophic component in each mode is determined as follows:

$$\tau_2 = \frac{V_y^{01} \cdot \sum_{i=1}^{n} V_{x_i} = V_x^{01} \cdot \sum_{i=1}^{n} V_{y_i}}{V_x^{01} \cdot V_y^{02} - V_y^{01} \cdot V_x^{02}} \cdot T_C \cdot \tag{5}$$

Then $\gamma = \frac{\tau_2}{T_C}$ & $\beta = 1 - \gamma$.

Determination of Mean Stationary Concentrations

Let us now consider the mean stationary values that the concentrations of carbon dioxide will assume, $\bar{y}_i$ $(i = \overline{1, n})$.

From (3b) [1] we have:

$$\bar{y}_i = \bar{y} - \frac{\bar{V}_y(\bar{y}) - V_{y_i}/\omega_i}{Q}. \tag{6}$$

Here, $\bar{y}$ is determined from the mandatory stability [stationary] conditions 2(b) [1].

Thus, the mean stationary values of carbon dioxide concentrations are unrelated to their initial values y_{0i}, but are determined only by the parameters of the closed ecological system. If the second mode I_2 is in the dark, the concentration of CO_2 in the general collector is determined by the equation:

$$\bar{y} = \frac{T_C \cdot \sum_{i=1}^{n} V_{y_i} - V_y^{02} \tau_2}{V_y^{01} \tau_1} - A. \tag{7}$$

Let us now turn to determination of mean stationary values of oxygen concentration, x_i ($i = \overline{1, n}$).

In the general case, systems (1a) and (1b) [1] must be solved together.

However, if the concentration of carbon dioxide is close to its mean stationary level, i.e., conditions (3b) [1] are virtually met, one can use the following approach.

According to equation (1a) [1], the concentration of oxygen in compartments can be established only after the concentration of carbon dioxide in them is established. For this reason, in order to determine the stationary concentrations of oxygen we shall examine equation (1a) [1] with already stationary levels of carbon dioxide.

Adding up the (1a) [1] for all "i" and considering the conditions of stability (3a) [1], we shall obtain:

Hence:

$$\sum_{i=1}^{n} W_i \cdot \bar{x}_i = \sum_{i=1}^{n} W_i \, x_{0i} = \text{const}$$

and

$$\sum_{i=1}^{n} W_i \cdot (\bar{x}_i - \bar{x}_{0i}) = 0, \qquad (8)$$

where $\bar{x}_i$ refers to initial conditions for oxygen concentrations in inhabited compartments.

We have from equation (3a) [1]:

$$\bar{x} + \frac{\bar{V}_x(\bar{y})}{Q} = \bar{x}_i + \frac{V_{x_i}}{Q \cdot \omega_i}, \quad i = \overline{1, n}.$$

Therefore, we can write down:

$$\bar{x}_1 + \frac{V_{x_1}}{Q \cdot \omega_1} = \bar{x}_2 + \frac{V_{x_2}}{Q \cdot \omega_2} = \dots = \bar{x}_n + \frac{V_{x_n}}{Q \cdot \omega_n}. \qquad (9)$$

By solving equations (8) and (9) together, we obtain the equations for determination of stationary values:

$$\bar{x}_i = \frac{\sum_{l=1}^{n} W_l \cdot \bar{x}_{0l} + \frac{1}{Q} \cdot \sum_{j=1}^{n} \left(\frac{V_{x_j}}{\omega_j} - \frac{V_{x_i}}{\omega_i} \right) \cdot W_j}{\sum_{l=1}^{n} W_l}; \qquad (10)$$

$$l \neq i; \; i = \overline{1, n}.$$

We see from equation (10) that the stationary concentrations of oxygen x_i depend on the initial conditions.

Thus, with $n = 1$, the mean stable concentration $\bar{x}_1$ will be its initial level, x_{01}. With $n>2$, the stable concentrations x_i will be different from their initial values in the general case.

Let us mention that the results obtained above for $n = 1$ are entirely consistent with the conclusions in [2], in which a system with one compartment is studied.

First example: Let us consider an ecological system, closed with regard to exchange of gases, with one habitable compartment and an autotrophic component that operates in light and darkness, with the following parameters corresponding to the data submitted in [2]:

$$V_{y_1} = 0{,}012\ \text{м}^3/\text{h};\ V_x^{01} = 0{,}0625\ \text{м}^3/\text{h};\ r^{01} = 0{,}85;$$
$$r^{02} = 1;\ \ V_x^{02} = -0{,}0074\ \text{м}^3/\text{h};\ V_y^{01} = 0{,}0531\ \text{м}^3/\text{h};$$
$$V_y^{02} = -0{,}0074\ \text{м}^3/\text{h};\ W = 20\ \text{м}^3;\ T_C = 23\ \text{h}.$$

In order to satisfy the necessary and sufficient conditions for stability of a closed ecological system, let us take 0.82 as the coefficient of respiration of the heterotrophic components [3]. Then the rate of O_2 uptake by the heterotrophic components will be $V_{x_1} = 0.0146\ \text{m}^3/\text{h}$. For this system, we have to define the parameters of programmed control that would provide for stable, periodic changes in concentrations of O_2 and CO_2, as well as the mean stable value for CO_2.

The control parameters τ_1 and τ_2, which were calculated using formulas (1) and (2) constitute 14.7 and 8.3 h, respectively.

The mean stationary value of CO_2 is 0.68%.

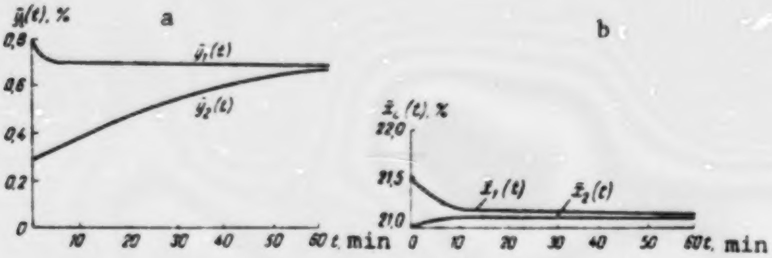
For the sake of comparison, let us mention that the values for control parameters defined in [2] are very close to the ones we calculated, constituting $\tau_1 = 15$ h and $\tau_2 = 8$ h.

Second example: Let us consider an ecological system with two habitable compartments and the same autotrophic component as in the first example, which operates in the light and darkness, with the following parameters:

$$V_{x_1} = 0{,}004\ \text{м}^3/\text{h};\ V_{x_2} = 0{,}008\ \text{м}^3/\text{h}\ V_{y_1} = 0{,}00328\ \text{м}^3/\text{h};\ V_{y_2} = 0{,}00656\ \text{м}^3/\text{h};$$
$$V_x^{01} = 0{,}0625\ \text{м}^3/\text{h};\ V_x^{02} = -0{,}0074\ \text{м}^3/\text{h};\ V_y^{01} = 0{,}0531\ \text{м}^3/\text{h};\ V_y^{02} = -0{,}0074\ \text{м}^3/\text{h};$$
$$W_1 = 5\ \text{м}^3;\ W_2 = 15\ \text{м}^3;\ \omega_1 = 0{,}333;\ \omega_2 = 0{,}667;\ \bar{x}_{01} = 21{,}5\%;\ \bar{x}_{02} = 21\%;$$
$$\bar{y}_{01} = 0{,}8\%;\ \bar{y}_{02} = 0{,}3\%;\ T_C = 2\ \text{h}.$$

We need to calculate the program for control of the autotrophic component.

According to (10), the stationary values for oxygen, $\overline{x}_1$ and $\overline{x}_2$, are the same and equal 21.125%.



Concentrations of carbon dioxide $\overline{y}_1(t)$ and $\overline{y}_2(t)$ (a) and oxygen $\overline{x}_1(t)$ and $\overline{x}_2(t)$ (b) as a function of time after turning on the programmed control system

The stationary values for carbon dioxide (7) are $\overline{y}_1 = \overline{y}_2 = 0.68\%$.

Taking into consideration formula (1), operating time in mode I_2 is $\tau_2 = 0.716$ h, and in mode I_1 $\tau_1 = 1.284$ h.

The Figure illustrates the curves of changes in oxygen and carbon dioxide concentrations after turning on the system of programmed control.

BIBLIOGRAPHY

1. Nasonov, A. S., and Toroptsev, V. S. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1979, pp 63-68.
2. Shabel'nikov, V. G. Ibid, No 6, 1975, pp 36-40.
3. Smirnov, I. V. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 19, 1972, pp 90-180.

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EFFECT OF SODIUM BICARBONATE ON REACTIVITY AND TROPHICS OF VESTIBULAR ANALYZER

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1980 pp 64-68

[Article by N. I. Arlashchenko, submitted 20 Jan 77]

[English abstract from source]

Prevention of motion sickness by intravenous injections of sodium bicarbonate may be a direct result of trophic changes or effect of the chemical on the functional activity of central formations.

[Text] Hasegawa was the first to demonstrate on rabbits and man [1], in 1949, that sodium bicarbonate prevents signs of motion sickness when injected intravenously to animals and man; this was confirmed in subsequent studies [2-4]. However, the mechanism of preventive action of sodium bicarbonate is not clear to this day. At any rate, dissolution of otoliths in the labyrinthine vestibulum, as assumed by Hasegawa [2], does not occur, and this was proven [5] by means of an original technique for making a preparation of the vestibular system, which precludes the use of decalcification, which is inevitable with the usual techniques for making preparations of the inner ear [6]. Perhaps, depression of autonomic reactions occurs as a result of elevation of threshold of stimulation of chemoreceptors of the trigger zone in the vomiting center, demonstrable by the increase in threshold of apomorphine vomiting in dogs after administration of sodium bicarbonate [7]. Some authors [4] believe that prevention of signs of motion sickness (nausea, vomiting, hyperhidrosis and other manifestations of motion sickness) after administration of sodium bicarbonate is attributable to normalization of hemodynamics, increase in alkaline reserve of blood and improved tissular oxygenation.

Our objective here was to study the mechanism of the effect of sodium bicarbonate on the vestibular analyzer.

Methods

The presence of a barrier mechanism in the inner ear, which provides for relative stability of chemical composition of labyrinthine fluid, has been proven by several researchers, who observed limited penetration of various dyes and radioactive tracers from blood into the lymph of the ear [8-9]. Experiments on dogs and cats [8] proved that such specialized vasotissular barriers as the hematolabyrinthine (HLB), hematoophthalmic (HOB) and hematoencephalic (HEB) barriers are equally permeable to labeled phosphorus. Experiments on rabbits [9] established that there is equally limited permeability of the same barriers for fluorescein. As a rule, studies of barrier function of the HLB are conducted in the form of acute experiments, with collection of perilymph from the labyrinth. For this reason, we tested permeability of the HOB as a model that would enable us to make a judgment about disturbances in permeability of specialized vasotissular barriers in the course of a chronic experiment. The transparency of the internal media of the eye makes it possible to directly observe and objectively record penetration of intravenously injected fluorescein (0.5 cc 5% solution per kg weight) into the lymph of the anterior chamber of the eye. The intensity of fluorescence of fluorescein in the humor of the chamber was measured in relative units with a luminescence microphotometer for 3.5 h after injection of the dye [10]. In our experiments, permeability of the HOB in rabbits examined under normal conditions and 2 h after total-body γ-irradiation from a cesium source, in a dose of 700 R at the rate of 37 R/min, served as an indicator of normal "physiologically adequate" [11] and pathological "physiologically inadequate" permeability of the vasotissular barrier. We gave the rabbits intramuscular injections of ethaperazine, in a dosage of 1 mg/kg weight, 10-15 min prior to exposure to radiation, in order to determine the nature of changes in permeability of the vasotissular barrier under the influence of factors aimed at the reticular formation.

We tested vestibular function by means of a VU-2 type device [12] with an electronic control console. We rated the hystagmic and respiratory reactions to stop stimuli of 5, 7, 10, 20, 30, 40, 60 and 90° per second, in several background studies and 20-30 min after intravenous injection of sodium bicarbonate (15 mℓ 5% solution). After this, to enhance the quality of histological treatment and demonstration of early morphological changes in the labyrinth, we performed in vivo fixation of the labyrinths based on replacement of the animal's blood with Vitmak fluid. The temporal bones with fixed labyrinths were extracted from the skull and submitted to histological treatment (fixation in Vitmak fluid for 3 weeks at a temperature of 37°C, decalcification in 5% nitric acid solution to a specific degree of softening, neutralization in 10% sodium sulfate, flushing, dehydration in alcohols, embedding in celloidin, preparation of serial sections and staining thereof with hematoxylin-eosin).

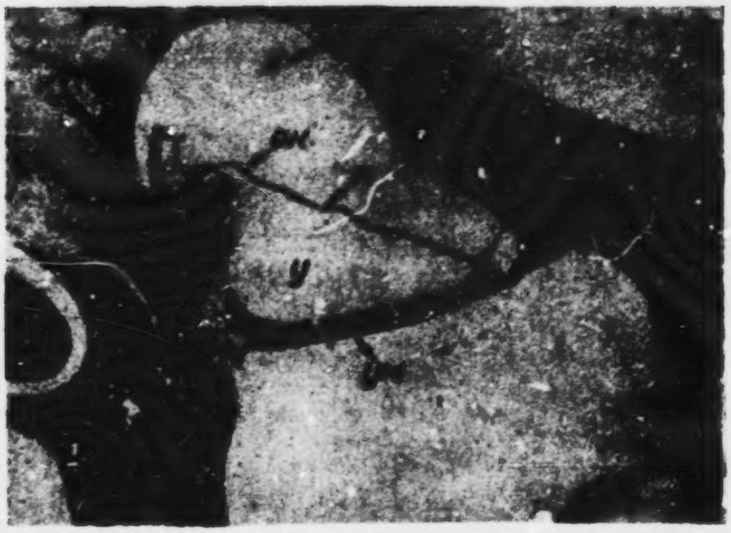

Figure 1. Histology of the labyrinth after intravenous injection of sodium bicarbonate. We see the collapse of the walls of the membranous labyrinth (n) on the level of the utricular sac (y) and ampulla of the semicircular duct (a). Normally, the membranous labyrinth has the same shape as the osseous (k); hematoxylin-eosin stain; magnification 3.5×7

ak) ampullar crista ym) utricular macula

In all, we used 42 rabbits in different series of experiments. The data obtained in the experiments were submitted to statistical processing.

Results and Discussion

The morphology of the inner ear after injection of sodium bicarbonate (Figure 1) indicates that there is some degree of compression of the membranous labyrinth, collapse of the walls of the utricular sac so that they are in contact with the sensory receptor epithelium of the crista.

Figure 2 illustrates the levels of normal permeability of the HOB before and after injection of sodium bicarbonate and pathological permeability of the vasotissular barrier as a result of exposure to ionizing radiation. Injection of sodium bicarbonate 10-15 min before irradiation altered the signs of radiation destruction of the vasotissular barrier, leading to slower migration of fluorescein into the humor of the chamber. Delayed passage of the tracer into the lymph of the anterior chamber of the eye was also observed when the animals were given ethaperazine 10-15 min before irradiation.

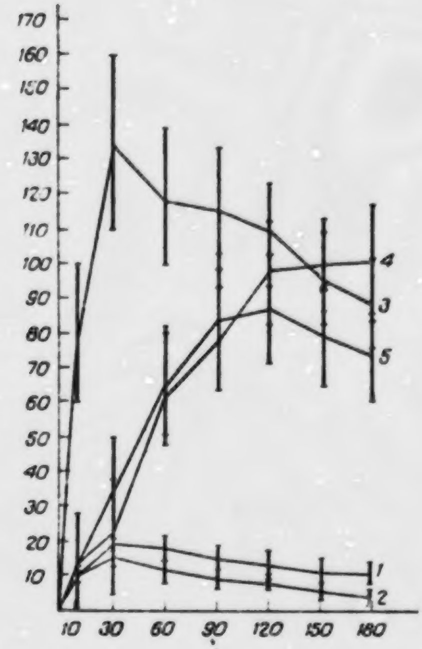

Figure 2.
Permeability of HOB for intravenously injected fluorescein. X-axis, time after injection of fluorescein (min); y-axis, intensity of fluorescence of fluorescein in chamber humor (in relative units)

1) normal
2) against the background of sodium bicarbonate
3) 2 h after irradiation
4) after irradiation, against the background of sodium bicarbonate
5) after irradiation, against the background of ethaperazine

Depression of the nystagmic reaction was somewhat more marked after administration of sodium bicarbonate than as a result of conditioning by means of background rotation. Processing by the differential method revealed reliable differences in reactions to stop stimuli of 30, 40 and 90° per second before and after administration of sodium bicarbonate. There were also appreciable changes in respiration reaction to stop stimuli of 40, 60 and 90° per second under the influence of sodium bicarbonate (see Table).

It can be assumed that the endolymph is a nutrient medium for labyrinthine receptors, since the latter have no direct contact with the system of blood vessels [13]. For this reason, the slightest change in electrolyte composition of ear lymph, due to impairment of the vasotissular barrier, should affect the function of vestibular receptors. The possibility of using HOB indices to test the barrier function of the HLB is based on the coincidence of levels of permeability of both vasotissular barriers to intravenously injected fluorescein [8, 9]. Penetration of fluorescein and sodium salt of fluoresceinic acid is indicative also of the possibility of passage through vasotissular barriers of very small amounts of other sodium salts under normal conditions, including sodium bicarbonate.

Respiratory reaction to stop stimuli (10-s interval) in background studies and 20-30 min after injection of sodium bicarbonate (% of number of respiratory excursions before stop stimulus)

Nature of rotation	Magnitude of stop stimulus, degrees/s					
	20	30	40	60	90	120
Background, first	101±2	100±2	99±1	88±3	89±2	80±8
Background, second	100±1	99±2	92±4	88±4	88±4	80±11
Background, third	100±1	101±2	98±3	98±4	102±5	109±6
After injection of sodium bicarb.	99±7	108±4	121±5	128±7	121±7	—

The endolymph has the same proportion of electrolytes as intracellular fluid, in particular, there is an exceptionally high potassium content. The perilymph, in which there is prevalence of sodium ions, is closer to blood in composition of electrolytes. For this reason the appearance of an excess of sodium cations in perilymph after administration of sodium bicarbonate could increase efflux of fluid and endolymph, and it could lead to elevation of osmotic pressure of perilymph and compression of the membranous labyrinth. Evidently, compression of the latter after intravenous injection of sodium bicarbonate is indicative of normally present osmotic equilibrium of endolymph and perilymph. We observed even more marked compression of the membraneous labyrinth after exposure of animals to total-body γ-radiation [14]. It is known that ionizing radiation destroys specialized vasotissular barriers [15-17]. Along with drastic increase in permeability of the vasotissular barrier, which is observed 2 h after exposure to ionizing radiation [18, 19], there are also marked changes in excitability and reactivity of the vestibular analyzer, as manifested by elevation of threshold of perception of angular accelerations, attenuation and reduction of duration of nystagmic reaction to stop stimuli [20-22]. Evidently, both a change in electrolyte composition of ear lymph and a change in intralabyrinthine pressure of liquid media, which occurs as a result of impairment of the HLB, may be the source of peripheral afferent influences capable of altering the sensitivity of the vestibular analyzer to vestibular stimuli. It is also possible that these trophic disorders attenuate the vegetovestibular manifestations of motion sickness under the influence of sodium bicarbonate.

The change in nature of radiation damage to the vasotissular barrier against the background of sodium bicarbonate is manifested by slower passage of the dye into the humor of the chamber, appearance of a "flat" curve of dynamics of pathological permeability of the vascular barrier. Preliminary administration of ethaperazine had exactly the same effect on the nature of pathologically increased permeability of the vascular barrier with exposure to radiation. In view of the fact that ethaperazine affects the same structures of the central nervous system as aminazine [23], and in view of the fact that the shape of the curves of pathological permeability was the same under the influence of sodium bicarbonate and ethaperazine, it may be assumed that sodium bicarbonate influences the functional state of the brain stem. In particular, the shift of blood pH as a result of administration of large amounts of anion of carbonic acid, as indirectly indicated by changes in the respiratory reaction to stop stimuli after injection of sodium bicarbonate, could be the active factor. Evidently, the so-called extralabyrinthine nature of effect of sodium bicarbonate on the vestibular analyzer consists of the above mediated influence on the central stem formations of the nervous system.

Thus, as a result of these experiments, it was established that intravenous injection of sodium bicarbonate has an appreciable effect on functional activity of the vestibular analyzer, attenuating nystagmic and distorting respiratory reactions to stop stimuli. On the basis of the obtained data, it can be assumed that, when injected intravenously, sodium bicarbonate influences primarily the liquid media of the labyrinth, disrupting osmotic equilibrium of endolymph and perilymph, and leading in some cases to compression of the membranous labyrinth. Aside from its direct effect on labyrinthine trophics, sodium bicarbonate also affects the body via the vegetative centers, as indicated by the analogy of effects of pathologically increased permeability of the vasotissular barrier after administration of sodium bicarbonate and ethaperazine. Thus, the changes in vestibulosomatic and vestibulovegetative reactions to stop stimuli, which occur after intravenous injection of sodium bicarbonate, could be the result of both the direct trophic influence on the peripheral part of the vestibular analyzer and the extralabyrinthine effect via the higher vegetative centers. The described mechanisms probably explain the distinctions of the effect of sodium bicarbonate on vestibulovegetative manifestations of motion sickness.

BIBLIOGRAPHY

1. Nasegawa, T. ARCH. OTOLARYNG., Vol 50, 1949, p 708.

2. Idem, ARCH. OHR.-NAS. U. KEHLK.-, HEILK., Vol 166, 1955, p 319.

3. Barnatskiy, V. N., and Kuznetsov, A. G. KOSMICHESKAYA BIOL. [Space Biology], No 1, 1968, p 49.

4. Barnatskiy, V. N.; Bryanov, I. I.; Volosevich, R. M.; et al. Ibid, No 6, 1972, p 70.

5. Vinnikov, Ya. A.; Lukashevich, T. T.; and Zhinkin, I. L. VESTN. OTORINOLAR. [Vestnik of Otorhinolaryngology], No 5, 1964, p 72.

6. Vinnikov, Ya. A., and Titova, L. K. ARKH. ANAT. [Archives of Anatomy], No 4, 1959, p 82.

7. Syabro, O. I. "Studies of Pharmacology of Antiemetics," author abstract of doctoral dissertation, Leningrad, 1965.

8. Zayko, N. N. DOKL. AN SSSR [Reports of the USSR Academy of Sciences], Vol 102, No 4, 1955, p 831.

9. Yershov, V.I. TRUDY VOYEN.-MORSK. MED. AKAD. [Works of the Naval Medical Academy], Vol 34, 1952, p 36.

10. Gromov, V. A., and Nakhil'nitskaya, Z. N. in "Sbornik referatov po radiatsionnoy meditsine za 1958 god" [Collection of Abstracts on Radiation Medicine for 1958], Moscow, 1959, p 154.

11. Rosin, A. Ya. in "Fiziologiya i patologiya gistogematicheskikh bar'yerov" [Physiology and Pathology of Blood-Tissue Barriers], Moscow, 1968, p 10.

12. Grigor'yev, Yu. G., and Bokhov, B. B. VESTN. OTORINOLAR., No 6, 1961, p 85.

13. Mayerovich, I. M. "The Hematolabyrinthine Barrier," Leningrad, 1973.

14. Shikhodyrov, V. V.; Arlashchenko, N. I.; and Grigor'yev, Yu. G. RADIOBIOLOGIYA [Radiobiology], No 4, 1971, p 560.

15. Kiselev, P. N. "Effect of X-Rays on Permeability and Barrier Functions of Body Tissues," author abstract of doctoral dissertation, Leningrad, 1951.

16. Shtern, L. S.; Rapoport, S. Ya.; Gromakovskaya, M. M.; et al. BIOFIZIKA [Biophysics], No 2, 1957, p 187.

17. Kassil', G. N. "The Hematoencephalic Barrier," Moscow, 1963.

18. Arlashchenko, N. I. MED. RADIOL. [Medical Radiology], No 3, 1956, p 29.

19. Idem, OFTAL'MOL. ZH. [Ophthalmological Journal], No 4, 1961, p 233.

20. Sveshnikov, A. A. MED. RADIOL., No 9, 1963, p 48.

21. Sevan'kayev, A. V. in "Aviatsionnaya i kosmicheskaya meditsina" [Aviation and Space Medicine], Moscow, 1963, p 431.

22. Grigor'yev, Yu. G.; Farber, Yu. V.; and Volokhova, N. A. "Vestibular Reactions," Moscow, 1970.

23. Mashkovskiy, M. D. "Drug Products," Moscow, 8th edition, Vol 1, 1977, p 51.

CLINICAL STUDIES

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EVALUATION AND FORECASTING OF MENTAL FITNESS OF FLIGHT PERSONNEL IN THE PRESENCE OF NEUROSIS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1980 pp 68-72

[Article by K. K. Ioseliani, submitted 23 Jan 78]

[English abstract from source]

Features of psychic functions and mental performance of flight personnel suffering from various neuroses were examined by clinical and psychological methods. The most severe and persistent changes in mental performance were found in neurasthenics. Higher mental productivity was detected in 80 % of subjects with other neuroses (neurotic states and reactions, asthenic state, emotional-vegetative instability) ($P<0.001$). These findings can be regarded as important diagnostic and prognostic criteria in expertise and performance evaluations.

[Text] Adverse flight factors lead, in some cases, to disruption of the correlation between excitatory and inhibitory processes in the central nervous system (CNS) and are instrumental in development of neurosis [1]. A number of Soviet researchers [1-4] have reported that in 40-50% of the cases development of neurosis among flight personnel is related to the most dangerous and stressful segments of flight (worsening of well-being, illusions, accident situations, erroneous actions, loss of spatial orientation, etc.). Some of the characterological personality traits (impressionability, anxiety, accentuated self-confidence, stubornness), which prevent overcoming difficulties and complicate vital situations are also instrumental in development of neurosis [5-8].

There has been no general recognition of methods of clinicopsychological testing (CPT) in diagnostics and expert evaluation of fitness for work in the presence of neurosis, and in some cases they are even disputed, although prominent specialists in medical psychology believe that they can be used to obtain important information that supplements the findings of clinical examination [5, 9, 10].

In the last few years, psychologists, psychoneurologists and psychiatrists have shown great interest in personality tests and questionnaires that have been adopted from foreign practice [11, 12]. However, it is difficult to use these tests, since each of them involves a certain system for interpreting the results, which bears the influence of the conceptions of personality that are developed by their authors. Moreover, the existing level of the technique for interpretation of results does not assure adequate reliability of conclusions and total independence thereof from the experimenters [9].

In our opinion, the methods of clinicopsychological testing,* which make it possible to demonstrate the structure, nature and extent of mental disturbances, individual psychological distinctions and functional capability of flight personnel under model conditions, best meet the pressing need for psychological determination of fitness in the presence of neurosis for purposes of expert medical flight certification (EMFC).

Neuroses are in first place among all diseases of the nervous system in flight personnel, and they are the most frequent cause of occupational disqualification [1-4, 13]. For this reason, it is an important task for psychologists and expert neuropathologists to study the nature of functional disturbances in these individuals (including mental functions, fitness for work and behavioral reactions) in order to predict professional reliability.

It should be noted that the early stages of functional diseases of the CNS are seldom associated with marked impairment of mental fitness, and this is what causes difficulties in diagnosing them and making an expert judgment [1, 14]. In such cases, the results of CPT could play an important role as a diagnostic and prognostic criterion of performance reserve of flight personnel.

We failed to encounter such data about flight personnel in the available literature, and this served as grounds to conduct special studies in this direction.

In this work, we submit the results of our study of the dynamics and structure of the main mental functions and mental fitness of flight personnel suffering from neurosis, for the purpose of predicting professional reliability.

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*In essence, psychological examination of flight personnel for EMFC purposes is also the content of clinicopsychological examinations, since they constitute one of the components of a comprehensive work-up that is conducted for diagnostic and expert certification purposes.

Methods

We used the following techniques: "continuous counting in a specified tempo" to test emotional stability during performance; "retrieval of numbers, with switch-overs" (modification of F. D. Gorbov [2]) to test noise stability [resistance to interferences] during performance of differentiated, complex activity; "determination of patterns" to test some aspects of thinking (sharpness, activity and flexibility of thinking, critical attitude, capacity to establish consistent correlations, etc.); "compasses" for testing reproductive thinking and capacity to operate with spatial conceptions; "text reproduction" to test logical memory. This route of examination of individual psychological distinctions of the pilot's personality, which is being developed primarily by aviation psychologists [1, 2, 13, 14], is based on creating a model situation that reproduces different aspects of the difficult conditions of flight work.

The conclusion about the fitness level (high, average, low) was made only after summarizing the results of all of the methods used according to specially developed criteria on a 9-point scale [14].

A total of 100 people (81 pilots and 19 navigators) were submitted to the testing; they had been referred for in-hospital examination and to settle a question of expertise due to diminished performance, fatigability during flights, irritability, sleep disorders, depressed affect, pain in various organs, etc. For the sake of comparison and analysis of CPT results, we also examined essentially healthy flight personnel (100 people) who made up the control group.

Results and Discussion

Experimental data obtained on the control group served as the base criterion in analyzing the CPT results.

The control group of subjects gave the impression of being collected, concentrated and sharp [quick-witted] people (88 of them had a high level of performance and 12 an average level). Their mental fitness was characterized by the following features: high initial readiness, manifested by good productivity at the first stage of a long work period; rapid adjustment, manifested by finding an adequate work procedure; transition from the elementary stage of coping exogenously specified rules to interiorized procedures, rapid development and readjustment of mental work skills; uniformity and stability of rate and rhythm of performance; commensurate interaction of voluntary and automated elements of performance and adequate change in procedures; smooth change from visual to mental level of performance and use of the latter as the refined work procedure; creative thinking; clearcut performance of intensive mental work when there is a shortage of time and exposure to informational interference;

fine differentiation of performance at the difficult stages of an assignment; critical attitude; insignificant (latent) manifestation of fatigue at the end of a long work period.

As a result of the comprehensive (clinical, instrument and clinicopsychological) examination of individuals in the main group, the following forms of neurosis were diagnosed: neurasthenia in 55 cases; neurotic states and reactions in 16; asthenic state in 10 and emotional vegetative instability in 19 people.

In order to graphically follow some of the distinctions and relationship between changes in mental functions and fitness for work occurring in response to various forms of neurosis, and for the sake of convenience in comparing these changes, it is deemed expedient to consider them in two subgroups differing in findings: the first subgroup consisted of individuals suffering from neurasthenia (55 people) and the second, all the rest of the individuals in the main group (45).

The patients in the first subgroup were characterized by marked emotional instability, conflict, exhaustibility, fixation on their sensations, depressed affect, sleep and memory disorders. There was a significant decline in mental work fitness. Of this subgroup, 27 people had difficulty in performing their assignments throughout the work period; they also made mistakes, particularly when there was a shortage of time and when switching to the opposite mode of work. Marked exhaustibility of mental functions, lack of the necessary readiness for performance of current work and disorganization of mental activities were found in 28 individuals, who scored the lowest in performance. In view of the severe worsening of well-being, 19 people had to stop the work. They usually stopped working after the work rate slowed down and number of mistakes, which became more and more flagrant, increased. Some subjects developed distinctive memory "lapses" (they forgot the instructions to follow in their work, current result of counting, direction [sign] of action, etc.) when there was a tight schedule. This was indicative of marked impairment of the elements of the complex functional structure that are usually related to phenomena referable to immediate recall [operative memory]. During complex differentiated activity ("retrieving numbers with switchovers") there was more frequent perseveration, impairment of color differentiation and significant divergence of series. Impairment of cognitive processes was noted in the "compass" and "establishment of patterns" tests.

All 55 subjects in the 1st subgroup were deemed unfit for flight work by the VLK [medical commission for determination of flight fitness].

The second subgroup of subjects was characterized by some emotional instability, increased fatigability and perspiration, superficial sleep. Against the background of an uneven work pace, moderate nervous tension and heightened emotional reaction to an experimental situation (facial vasomotor activity, systemic and palmar hyperhidrosis, faster pulse, etc.), the subjects presented much better results in the CPT for mental fitness than the first subgroup (see Table). After generalization of the obtained data, it was established that 19 people had a high score, 21 average and 5 low. The individuals in this subgroup were characterized by rather high degree of conditioning, which was indicative of structural integrity of their mental performance. It should be noted that the rather high productivity of these individuals was achieved at the price of enlisting their internal reserves.

Comparative CPT results for individuals in the 1st and 2d subgroups

Subgroup	Number of subjects	Performance level, %		
		High	Average	Low
First	55	--	49±9.5	51±9.5
Second	45	42±11.3	47±10.9	11±10.3
Totals	100	19±7.2	48±7.2	33±8.1

Note: Reliability of differences between performance rating for subjects in first and second subgroups with $P<0.01$.

The individuals in the main group, who suffered from neurosis, presented a statistically reliable discrepancy in mean performance scores ($P<0.001$), as compared to the control group.

The CPT results, along with the clinical findings and results of other functional load tests, made it possible to resolve the expert question in the affirmative in 31 cases, deeming subjects to be conditionally fit for flight work, thereby retaining personnel for aviation. In 69 cases the expert judgment was negative (see Table).

It is important to note that all of the 33 individuals who had low scores in the CPT were deemed unfit for flight work, while all 19 who had high performance scores were allowed to continue with their flying activities, although there were some restrictions.

These studies revealed that CPT methods make it possible to determine the correlation between efficiency of solving psychological problems, on the one hand, and clinical manifestation of disease, on the other. This enables us to assess the obtained indices as important diagnostic and prognostic criteria of professional fitness of flight personnel. This set of methodological procedures may aid in more differentiated evaluation of the severity of neurosis, with respect to conformity of the psychological and functional capabilities of a pilot with the requirements stipulated by the VLK.

BIBLIOGRAPHY

1. Gorbov, F. D. in "Obshchestvo psikhologov SSSR. S"yezd 3-y. Materialy" [Society of USSR Psychologists, Proceedings of 3d Congress], Moscow, Vol 3, Vyp 1, 1968, pp 115-117.

2. Idem, in "Inzhenernaya psikhologiya" [Engineering Psychology], Moscow, 1964, pp 340-357.

3. Mishurin, V. M. VOYEN.-MED. ZH. [Military Medical Journal], No 2, 1959, pp 62-67.

4. Severskiy, A. I. "Treatment and Prevention of Neurosis Among Flight Personnel," Moscow, 1965.

5. Myasishchev, V. N. "Current Conceptions of Neuroses," Moscow, 1956.

6. Davidenkov, S. N. "Neuroses," Leningrad, 1963.

7. Bamdas, B. S. "Asthenic States," Moscow, 1961.

8. Svyadoshch, A. M. "Neuroses and Their Treatment," Moscow, 1959.

9. Karvasarskiy, B. D., and Iovlev, B. V. in "Kliniko-psikhologicheskiye issledovaniya lichnosti (v svyazi s zadachami profilaktiki, diagnostiki i lecheniya nervno-psikhicheskikh zabolevaniy)" [Clinico-Psychological Personality Tests (Related to Prevention, Diagnosis and Treatment of Mental Diseases)], Leningrad, 1971, pp 43-47.

10. Tonkonogiy, I. M. Ibid, pp 72-75.

11. Karandasheva, E. A., and Kister, T. P. Ibid, pp 150-153.

12. Dneprovskaya, S. V. Ibid, pp 116-119.

13. Platonov, K. K. "Psychology of Flight Work," Moscow, 1960.

14. Ioseliani, K. K. "Clinico-Psychological Tests in the Practice of Medical Flight Expertise," author abstract of doctoral dissertation, Moscow, 1975.

BRIEF REPORTS

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DYNAMICS OF STRESS REACTION OF RATS DURING EXPERIMENTAL HYPOKINESIA VARYING IN DURATION, AND POSSIBILITY OF CORRECTION THEREOF

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1980 pp 72-74

[Article by L. Y. Kirichek, submitted 12 Jun 78]

[Text] It is known that, along with other factors, prolonged restriction of muscular activity plays an important role in development of the hypokinetic syndrome [1-3]. There are indications in the literature that hypokinesia first leads to a stress reaction, which is then followed by a period of adaptation, after which a state develops that characterizes the effect of hypokinesia as such [4-7].

Our objective here was to track the dynamic intensity of the stress reaction in rats as a function of time of restriction of movement, to determine the time of maximum manifestation of stress and demonstrate the nature of change therein under the influence of some central neurotropic agents.

Methods

Experiments were conducted on 210 mongrel white rats of both sexes, with an initial weight of 100 to 200 g, which were separated into groups of 6 animals. Hypokinesia was produced by means of special box cages made of plexiglas, which drastically restricted movement, but did not make routine care of the animals difficult. All of the animals were fed the same diet and maintained under the natural conditions of day and night. Hypokinesia lasted for 1 to 24 h and 1 to 30 days, with recording of parameters every hour for the first 6 h, then 12 and 24 h for the first 3 days of the experiment, on the 5th, 7th and 19th days, and every 5 experimental days thereafter. The weight coefficients of the thymus and adrenals, ascorbic acid content of the adrenals [8], blood eosinophils, incidence and intensity of onset of an ulcerative process in the stomach [9]. In addition, we recorded the rats' weight before and after hypokinesia, as well as death rate. Vivarium animals (20 rats in a cage with a 45×45 cm^2 floor) served as a control. We used psychotropic depressants as products for pharmacological correction of stress: reserpine (1-2.5-5 mg/kg by mouth) and amizil (1-2.5-5 mg/kg by hypodermic injection), which were given once 2 h before the end of the period of hypokinesia and repeatedly over a 10-day period, 5 days before hypokinesia and for the entire period of hypokinesia (5 days). In this series of experiments, rats given isotonic solution of sodium chloride under analogous conditions served as a control. We used the parametric method of Student for statistical processing of digital data.

Results and Discussion

The obtained data revealed that hypokinesia induced changes characterizing development of stress in the rats. This was manifested by a decrease in weight coefficient of the thymus, hypertrophy of the adrenals, undulant changes in ascorbic acid level in the adrenals, decrease in blood eosinophils and appearance of trophic disturbances of the gastric mucosa, the incidence and severity of which also fluctuated. The severity of changes was dissimilar as a function of time for each of the parameters studied. First to change, after exposure for 1 h, was the adrenal ascorbic acid level, which declined. Subsequent changes in level thereof were phasic and reflected fluctuation of functional activity of the adrenals in the course of the entire experiment. Adrenal weight increased after 24 h of hypokinesia and then increased consistently up to the 15th day, after which it became stable. In the interval between the 2d h and 15th day of hypokinesia, there was a decline of weight coeffficient of the thymus. After the 15th day, this parameter increased and even exceeded the mean base level by the end of the experiment. On the 5th day of hypokinesia, there was a decrease in eosinophils, then their number began to grow again, and by the 30th experimental day it was double the control level. The trophic disturbances appeared early (after 1 h of hypokinesia) in the gastric mucosa, and they were manifested at first only by pallor and edema of the mucosa, distension and atonia of the gastric walls. Effusions of blood, erosions and ulcers appeared in the rat stomach after 12 h of hypokinesia and reached a maximum (mean grade of 2) on the 5th, 15th and 20th days. A comparison of the dynamics of all parameters studied revealed that the maximum changes were referable to the period between the 5th and 15th days of hypokinesia, after which restoration of parameters began. Accordingly, there was also a change in weight of the animals at these times: 19 and 18% drop, as compared to base levels, at first and then restoration toward the end of the experiment. There were no deaths of animals.

The experiments involving the use of drugs were conducted against the background of 5-day hypokinesia. Under these conditions, a single indose of reserpine enhanced the stress reaction, leading to more marked adrenal hypertrophy, even greater drop in adrenal ascorbic acid and blood eosinophil content, and increase in incidence of ulcers in the stomach. With the second intake of reserpine, this influence was less marked, or even combined with a decline of eosinopenia. The effect of amizil was manifested only when it was given repeatedly, and it was characterized by prevalence of attenuating influence on intensity of stress reaction indices. This was indicated by an increase in weight coefficient of the thymus, decline in adrenal ascorbic acid content, less marked decline of blood eosinophils and considerable drop in incidence of gastric ulcers.

Analysis of the obtained data and comparison thereof to those in the literature [10-13] revealed that the model of experimental hypokinesia that we used induced a stress reaction in rats, the manifestations of which were consistent, interrelated, synchronous and characterized by the presence of stages. The anxiety stage under such conditions had two waves of manifestation, in the first 5-6 h and on the 5th-15th days, which corresponds to the reactions to stressors described in the presence of hypokinesia [14] and two-component stress as the result of primary emotional stress and subsequent metabolic effect of restricted movement [10, 12]. On the whole, the time of maximum stress reaction coincided with the findings of other authors who studied the dynamics of changes in weight of the adrenals and thymus [13-16]. However, according to the same authors, intensification of functional activity of the adrenals occurred for the first 5-6 days of hypokinesia, after which there was adaptation followed by depletion, in spite of persisting hypertrophy of these glands. Evidently, this must be taken into consideration when choosing duration of hypokinesia for the purpose of studying the possibilities of drug correction. The presence of ulcers of the gastric mucosa throughout the experiment was indicative of the rather great "hardness" of the hypokinesia model we used. The nature of the effects of reserpine and amizil, which coincide with data in the literature pertaining to their use for other types of stress [17, 18] and used in a number of cases to interpret the mechanisms of neurohumoral regulation of the stress reaction [19], were indicative, on the one hand, of the fact that hypokinesia was associated with a stress reaction, the manifestation, course and regulation of which are similar to those associated with various extreme states and, on the other hand, that it is possible to search for protective agents for such conditions among the known agents with central neurotropic action (on the example of repeated administration of amizil).

BIBLIOGRAPHY

1. Kakurin, L. I. in "Fiziologicheskiye problemy detrenirovannosti" [Physical Problems of Deconditioning], Moscow, 1968, pp 34-43.

2. Kraus, H., and Raab, W. "Hypokinetic Disease," Springfield, 1961.

3. Lamb, L. E.; Stevens, P. M.; and Johnson, R. L. AEROSPACE MED., Vol 36, 1965, p 755.

4. Dolgun, Z. S.; Novikova, S. P.; and Shashkov, V. S. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1971, pp 12-16.

5. Tizul, A. Ya.; Sokolov, Ye. I.; Mdinaradze, Yu. S.; et al. SOV. MED. [Soviet Medicine], No 7, 1972, pp 147-148.

6. Razin, S. N., and Rychko, A. V. VRACH. DELO [Medical Record], No 5, 1976, pp 104-107.

7. Poppay, M.; Gekht, K.; and Morits, V. ZH. VYSSH. NERVN. DEYAT. [Journal of Higher Nervous Activity], No 2, 1974, pp 348-349.

8. Birch, R. W.; Harris, L. S.; and Ray, S. N . BIOCHEM. J., Vol 27, 1933, pp 590-594.

9. Hillyard, I. W.; Doczi, J.; and Kiernan, P. B. PROC. SOC. EXP. BIOL. (New York), Vol 115, 1964, pp 1108-1112.

10. Kovalenko, Ye. A.; Popkov, V. L.; and Kondrat'yev, Yu. I. PAT. FIZIOL. [Pathological Physiology], No 6, 1970, pp 3-9.

11. Kovalenko, Ye. A.; Mailyan, E. S.; Popkov, V. L.; et al. USPEKHI FIZIOL. NAUK [Advances in Physiological Sciences], No 3, 1975, pp 110-136.

12. Portugalov, V. V.; Il'ina-Kakuyeva, Ye. I.; Artyukhina, T. V.; et al. in "Eksperimental'nyye issledovaniya gipokinezii, izmenennoy gazovoy sredy, uskoreniy, peregruzok i drugikh faktorov" [Experimental Studies of Hypokinesia, Altered Gas Environment, Accelerations, G Forces and Other Factors], Moscow, 1968, pp 29-33.

13. Portugalov, V. V.; Il'ina-Kakuyeva, Ye. I.; Rokhlenko, K. D.; et al. in "Aviatsionnaya i kosmicheskaya meditsina" [Aviation and Space Medicine], Moscow, Vol 2, 1969, pp 163-167.

14. Sakharova, I. N. in "Povolzhskaya konf. fiziologov, farmakologov i biokhimikov. 4-ya. Materialy" [Proceedings of 4th Povolzh'ye Conference of Physiologists, Pharmacologists and Biochemists], Saratov, Vol 1, 1966, pp 158-160.

15. Yurgens, I. L., and Kirillov, O. I. KOSMICHESKAYA BIOL., No 4, 1972, pp 3-6.

16. Brekhman, I. I.; Yurgens, I. L.; and Kirillov, O. I. in "VNII fizicheskoy kul'tury. Sektor fiziologii sporta. Materialy za 1966 g." [Proceedings for 1966 of the All-Union Scientific Research Institute of Physical Culture, Sector for Physiology of Sports], Moscow, 1966, pp 15-25.

17. Vostrikov, M. S. SBORNIK NAUCH. RABOT VOLGOGRAD. MED. IN-TA [Collection of Scientific Papers of Volgograd Medical Institute], Vol 26, 1973, pp 153-155.

18. Yel'skiy, V. N. ANEST. I REANIMATOL. [Anesthesiology and Resuscitation], No 3, 1977, pp 50-53.

19. Shalyapina, V. G. PROBL. ENDOKRINOL. [Problems of Endocrinology], No 2, 1970, pp 60-64.

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EFFECT OF BRIEF ANTIORTHOSTATIC HYPOKINESIA ON BLOOD IMMUNOGLOBULIN CONTENT

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No 1, 1980 pp 74-75

[Article by N. N. Mukhina, V. V. Chestukhin, V. Ye. Katkov and A. P. Karpov, submitted 24 May 77]

[Text] As has been previously shown [1, 2], space flight conditions induce a change in immunoglobulin (Ig) levels in peripheral venous blood. In this study, we assayed proteins with antibody activity in blood samples from different organs, and we tested the effect on levels thereof of brief antiorthostatic [head-down] hypokinesia (ANOH), which simulates the acute period of adaptation to weightlessness.

Methods

Selective catheterization, with collection of blood samples from different parts of the cardiovascular system, was performed on male volunteers (6 subjects) before and after 5-day bed rest in antiorthostatic position, with -4.5°tilt of the head end. The subjects were catheterized on a Siemens (FRG) unit using two catheters simultaneously, one rigit venous catheter (Kurnand No 7) that was introduced after puncturing the ulnar vein into vessels of different organs under x-ray monitoring, and a soft arterial one that was left permanently in the radial artery.

IgA, IgG and IgM were assayed by the method of Mancini [3], using antisera prepared at the Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, and the standards of the Behringwerke Firm (FRG).

The obtained results were submitted to statistical processing by the method of pair-by-pair related variants of Student and Fisher, using Student's t criterion for statistical analysis.

Results and Discussion

Brief hypokinesia induced certain changes in distribution of Ig in the blood stream, which was characterized by several distinctions even in the base state (see Table).

Effect of ANOH (bottom row of figures) on Ig content (in mg%) in blood samples taken from different parts of the cardiovascular system (M±m)

Blood	IgA	IgG	IgM
Arterial	357,5±38.8 335,0±32.8	1330.0±129.0 1281.6±105.9	136.3±15.0 131.2±9.4
Flowing from brain	429,1±32.0 310,8±38,8*	1253.3±198.4 1476.6±150.0	88.7±10.6 78.5±14.4
Flowing from liver	329,1±47.4 294,1±42,0	1663.3±134.9 1301.6±102.0*	131.7±9.5 138.5±6.8
Flowing from kidneys	351,6±37.2 340,8±38.4	1358.3±98.0 1423.3±22.2	128.3±8.5 132.8±8.4
Flowing from lower limbs	343,3±31.4 255,8±40,8*	1530.0±192.3 1208.3±108.5**	124.2±6.6 135.2±15.7
Mixed venous	337,5±78.3 304,2±34,0	1400.0±98.8 1366.6±104.3	134.8±9.7 127.8±9.7

* $P<0.05$.
** $P<0.01$.

Before ANOH, IgM level was lower and IgA level was higher in blood flowing out of the brain than in the systemic circulation (mixed venous and arterial blood; $P<0.05$); IgG level was higher in blood drained from the liver than in the systemic circulation ($P<0.05$).

After ANOH, we observed a decline of IgA content in blood flowing from the brain and lower extremities ($P<0.05$) and decline of IgG in blood draining from the liver and lower extremities ($P<0.05$).

There were even more appreciable differences in organic dynamics of the parameters, and we observed some new distinctions when we analyzed the changes ($P<0.05$) in their arteriovenous difference. We were impressed by the increase in arteriovenous difference for IgA for the brain (from -71.6 to +24.2 mg%) and IgG for the liver and lower extremities (-333.3 to -20.0 and -200.0 to +73.3 mg%, respectively). Conversely, the arteriovenous difference in IgG decreased for the brain (from +76.7 to -195.0 mg%). In other words, after ANOH the brain began to "capture" IgA from the blood flowing into it and "discharge" into the systemic circulation IgG, which in turn began to be "captured" by the liver and lower limbs.

Thus, this work dealt with organic distribution of the main classes of immunoglobulins, IgA, IgG and IgM, each of which is characterized by a number of distinctions. For example, IgA play the main role in protection of the gastrointestinal tract and tracheobronchial tree, and expressly they are the most susceptible to the influence of various deleterious factors [2]. IgG, which is present in the highest concentration in blood, consists of antibacterial and antiviral antibodies, as well as antitoxins, while IgM contains not only specific antibodies, but most natural antibodies (isoantibodies of the ABO blood group, cold agglutinins, rheumatoid factor, heterophil antibodies). We were impressed by the fact that IgM was the only class, the organic distribution of which was not affected by hypokinesia.

It is known that the lymph nodes and bone marrow are the main regions in which Ig synthesis occurs. For example, IgA is synthesized in the lymphoid follicles of the pharyngeal and palatine tonsils, as well as cells in the upper respiratory tract [4]. In addition, there are indications that the lymphoid follicles of the lungs and liver participate in Ig synthesis [5]. As shown by the results of our study, the brain and bone and muscle masses of the lower extremities play some role in the metabolism of these factors in healthy man; however, it is extremely difficult to assess the physiological significance of the demonstrated changes without additional studies.

One of the factors that influences immunological resistance of the organism is referable to changes in metabolism. If this is taken into consideration, the changes in Ig metabolism in the brain become more comprehensible, since substantial metabolic changes were inherent in this organ. In particular, we observed compensated metabolic acidosis, increase in activity of aspartate aminotransferase and β-lipoproteins in blood flowing out of the brain. These changes were much less marked in the lower extremities, or else they were completely absent; at the same time, the lower limbs were characterized more by changes in electrolyte metabolism and, first of all, Ca^{2+}, which plays an important role in formation of the immunological status [6].

In conclusion, it should be noted that our previous studies failed to demonstrate substantial changes in Ig of peripheral venous blood at such an early stage of bed rest. The results of the present study enable us to attribute this to the specifics of organic changes, which were not only dissimilar in extent, but in some cases in different directions. Of course, these differences were significantly leveled off in mixed venous blood, and this determined the relative stability of Ig levels in the systemic circulation.

Thus, brief hypokinesia induces in healthy individuals redistribution of levels of Ig in blood flowing out of different organs, while their levels in the systemic circulation did not change appreciably. Analogous studies, including some involving longer simulation of weightlessness, must be continued to confirm and provide a fuller explanation of the demonstrated changes, which had not been described previously in the literature.

BIBLIOGRAPHY

1. Mukhina, N. N. in "Aktual'nyye voprosy kosmicheskoy biologii i meditsiny" [Pressing Problems of Space Biology and Medicine], Moscow, Vyp 2, 1975, pp 150-152.

2. Fischer, C. L., et al. AEROSPACE MED., Vol 43, 1972, pp 856-859.

3. Mancini, G., et al. INT. J. IMMUNOCHEM., Vol 2, 1965, pp 235-254.

4. Fudenberg, H.; Pink J.; and States, D. M. "Introduction to Immunogenetics," 1975.

5. Prokopenko, L. G., and Ravich-Shcherbo, M. I. "Immunoglobulin Metabolism," Moscow, 1974.

6. Braun, W.; Ishizuka, M.; and Seeman, P. NATURE, Vol 226, 1970, pp 945-946.

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RAT PLASMA AND TISSUE LIPIDS AFTER A LONG-TERM SPACE FLIGHT

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[Article by J. Ahlers, R. A. Tigranyan, E. Ahlers, E. Paulikova and
M. Praslicka, submitted 21 Feb 78]

[Text] The studies conducted aboard Cosmos-605 and Cosmos-690 biosatellites revealed that when rats remain in weightlessness for a long time there are some changes in lipid metabolism [1, 2]. In view of the distinctions of the experiments, the studies were conducted 1 day after the biosatellites landed. In the experiment aboard Cosmos-782 biosatellite, the animals were examined directly at the landing site. In this way, we could have expected that there was no time for the metabolic changes inherent in weightlessness to become modified under the influence of returning to earth's gravity or during prolonged transportation.

Our objective here was to study the lipids of plasma and certain tissues of rats after completing a flight aboard Cosmos-782.

Methods

The studies were conducted on Wistar-SPF male rats 6-10 h and 26 days after completion of a 19.5-day experiment aboard Cosmos-782. The obtained data were compared to the results of studies on animals involved in a synchronous experiment and the vivarium control. We assayed nonesterified fatty acids (NEFA) [3] in blood plasma, the liver, white (epididymal) and brown fatty tissue (intercapsular); triglycerides (TG) [4] and phospholipids (PL) [5] in plasma, liver, thymus and bone marrow (humerus); and total cholesterol (Ch) in plasma and liver [6]. The obtained data were processed by the method of variational statistics with the use of the Duncan test [7].

Results and Discussion

After completion of the flight and synchronous experiments, NEFA concentration in blood plasma was significantly higher than in intact animals; these changes persisted only in animals in the synchronous experiment after 26 days. After completion of the experiment, plasma TG was also higher in aniamls of the flight and synchronous groups than the level observed in intact rats, and this elevation was more marked in the synchronous group; virtually no changes were noted after 26 days. Plasma Ch did not differ from the control in all of the examined animal groups, while plasma PL was appreciably lower in flight animals after the experiment than in the control, whereas in the synchronous group they were above the control levels after 26 days (Table 1).

Table 1. Composition of blood plasma and liver lipids

Time of study	Conditions of experiment	NEFA, meq/ℓ	TG, mg%	Ch, mg%	PL, mg%
		Plasma			
6-10 h after experiment	Intact control	688±98 (5)	107,6±11,5 (5)	110,2±7,9 (5)	189,8±6,8 (5)
	Synchron. exper.	1104±152* (6)	366,3±25,0** (6)	127,3±13,1 (5)	211,4±21,9 (4)
	Flight experim.	1392±233* (5)	231,8±28,3*** (5)	110,9±5,6 (5)	155,3±6,1*** (5)
26 days after experim.	Intact control	452±103 (4)	186,7±42,8 (3)	95,7±14,1 (5)	159,6±10,6 (5)
	Synchr. experim.	1376±133** (5)	156,3±11,1 (5)	106,7±6,1 (5)	198,5±6,9 (5)
	Flight experim.	1182±360 (4)	139,0±10,4 (5)	113,7±10,2 (5)	178,5±15,6 (5)
		Liver			
6-10 h after experim.	Intact control	3,74±0,48 (6)	15,73±0,85 (6)	4,33±0,23 (6)	33,4±0,64 (6)
	Synchr. experim.	3,92±0,44 (6)	26,05±1,53** (6)	4,29±0,25 (6)	35,4±1,34 (6)
	Flight experim.	5,91±0,75* (6)	26,53±2,00** (6)	4,89±0,22 (6)	33,4±0,96 (6)
26 days after experim.	Intact control	3,76±0,33 (4)	12,33±0,88 (6)	4,23±0,13 (6)	34,02±2,00 (5)
	Synchr. experim.	4,33±0,51 (4)	12,88±0,30 (6)	4,30±0,18 (6)	35,8±1,68 (6)
	Flight experim.	3,24±0,39 (6)	14,38±1,27 (6)	5,21±0,44 (6)	37,1±3,15 (5)

*P<0.05 **P<0.001 ***P<0.01

After the experiment, there was elevation of NEFA and TG in the liver of flight animals, as well as of TG in the synchronous group, as compared to the control; Ch and PL content did not change. Lipid content of the liver was the same 26 days after the experiment in flight and synchronous groups, as in control animals (the only exception was an elevated Ch level in flight rats; see Table 1).

In the thymus, an elevation of TG level was observed immediately after the experiment only in the synchronous group; we failed to demonstrate changes in TG content in the other groups of animals, or changes in PL content of all groups examined (Table 2).

Table 2. Composition of lipids of the thymus, bone marrow and fatty tissues

Time of study	Conditions	Thymus		Bone marrow		Fatty tissue	
		TG, mg/g	PL, mg/g	TG, mg/g	PL, mg/g	white	brown
						NEFA/ meq/g	
6-10 h after exper.	Intact control	43,5±8,5 (6)	13,8±0,19 (6)	84,7±12,3 (6)	20,0±1,39 (6)	3,29±0,57 (6)	2,45±0,49 (5)
	Synchr.exper.	82,4±10,2 (6)	13,6±0,24 (6)	103,3±14,0 (6)	24,3±1,09 (6)	6,89±1,15 (5)	10,54±2,27*** (6)
	Flight exper.	63,3±9,3 (6)	13,7±0,60 (6)	87,3±9,9 (6)	12,9±0,94*** (6)	10,00±0,75** (6)	18,75±1,62** (6)
26 days after exper.	Intact control	43,0±8,4 (6)	14,8±0,26 (5)	117,4±17,9 (6)	12,6±1,66 (6)	3,38±0,59 (5)	8,3±1,14 (6)
	Synchr.exper.	67,7±9,6 (6)	14,5±0,67 (6)	99,1±14,2 (6)	11,4±0,59 (4)	2,55±0,17 (6)	5,51±0,54 (6)
	Flight exper.	51,9±12,0 (6)	14,4±0,49 (6)	101,7±16,6 (6)	11,9±0,46 (6)	5,95±0,46*** (6)	15,75±1,44** (5)

TG and PL content of bone marrow of rats in all groups did not differ from control levels [the only exception was a significant decline of PL in flight animals immediately after the flight (see Table 2)].

NEFA concentration in white and brown fatty tissue was significantly above control levels in flight and synchronous animal groups, and the changes were more marked in the flight rats; after 26 days the concentration of NEFA continued to remain high in flight animals (see Table 2).

The obtained data indicate that there were changes in some parameters of lipid metabolism in rats examined immediately after completing a flight aboard the Cosmos-782 biosatellite. There were signs of increased lipolysis in fatty tissue and increased mobilization of lipids. These findings are particularly significant because we examined satiated animals. It should be noted that similar changes, but to a lesser extent, were also noted in animals in the synchronous ground-based experiment. When examined at the re-adaptation stage, i.e., 26 days after landing, there was increase in concentration of NEFA in white and brown fatty tissue in flight rats only, and in blood of the synchronous group of animals. As a result of increased mobilization of lipids, there was an increase in concentration of NEFA and TG in the liver of rats in the flight and synchronous groups, but it reverted to normal at the readaptation stage. There were minimal changes in metabolism of Ch, and they could be assessed only by examining Ch synthesis with the use of labeled precursors. It should be noted that plasma Ch of cosmonauts decreased during flights and did not change or decreased negligibly after them [8]. The main TG levels in bone marrow (humerus) were 3-4 times higher in all groups examined than the normal values we obtained for this tissue without significant deviations in different groups. The increased lipogenesis could be due to diet (high fatty acid, etc., content) or difference in lipid composition of rat bone marrow. For this reason, it would be desirable to examine animals that are not satiated in the future.

The changes in spectrum of plasma and tissue lipids under the influence of prolonged weightlessness cover a narrow range, and they are an expression of insignificant stress, which is well tolerated by the animals.

BIBLIOGRAPHY

1. Gayevskaya, M. S.; Ushakov, A. S.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1976, pp 25-29.

2. Ahlers, J.; Misurova, E.; Praslicka, M.; et al. in "Life Sciences and Space Research," Berlin, Vol 14, 1976, pp 185-188.

3. Dole, V. P., and Meinertz, H. J. BIOL. CHEM., Vol 235, 1976, pp 2595-2599.

4. Eggstein, M., and Kreutz, F. H. KLIN. WSCHR., Vol 44, 1966, pp 262-267.

5. Bartlett, G. R. J. BIOL. CHEM., Vol 234, 1959, pp 466-468.

6. Zlatkis, A.; Zak, B.; and Boyle, A. J. J. LAB. CLIN. MED., Vol 41, 1953, pp 486-490.

7. Duncan, D. B. BIOMETRICS, Vol 11, 1955, pp 1-42.

8. Balakhovskiy, I. S., and Natochin, Yu. V. "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 22, 1973, pp 89-194.

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FUNCTIONAL CHANGES IN THE ADRENAL CORTEX DURING SIMULATION OF STRESS SITUATIONS IN THE PRESENCE OF HIGH CARBON MONOXIDE LEVELS

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[Article by S. K. Kalandarov, V. P. Bychkov and V. P. Savina, submitted 16 Jan 78]

[Text] When man is confined to an airtight compartment, there is discharge and accumulation of toxic chemicals. One of the main ones is carbon monoxide (CO).

CO can accumulate in the air of a pressure chamber as a result of its constant discharge into the environment in the course of human vital functions. The rate of output of CO in exhaled air constitutes, according to the data of Sjostrand [1], 0.24 mg/h, which is considerably higher than the discharge of other microimpurities.

CO can also be discharged from polymers.

Significant elevation of CO level was noted in the case of brief malfunction of some elements of the life support system [2].

There are extremely few works dealing with the influence of CO on adrenocortical function. As a rule, such studies were conducted in the form of brief experiments (up to 6 h/day exposure to CO). Their findings are contradictory. Thus, some authors report an increase in adrenocortical function under the influence of CO [3, 5, 6], while others, on the contrary, report a decrease in activity [7, 8]. I. M. Peysakhovich [9] failed to demonstrate changes in adrenocortical function in animals with severe CO poisoning.

No studies have been made of the functional state of the adrenal cortex of man during a prolonged and continuous stay in a pressure chamber with high CO content, although it is known that a prolonged stay in an artificial atmosphere is a factor with independent biological significance, which contributes a number of distinctions to the effect of an altered gas environment on the body [10]. Nor have there been studies of the combined effect of CO in a high concentration, high temperature and humidity on the functional state of the human adrenal cortex during a prolonged stay in a pressure chamber.

We undertook this study for the purpose of preventing occurrence of such conditions in cabins of manned spacecraft.

Methods

We conducted 4 series of experiments in a 24 m^3 pressure chamber at normal barometric pressure. A total of 16 subjects, ranging in age from 22 to 36 years (4 in each series) participated in the studies. In the 1st and 2d series, we examined adrenocortical function with exposure to high levels of CO (20 and 15 mg/m^3, respectively). In the 3d series, we tested the effect on adrenocortical function of high CO content (15 mg/m^3) and more difficult conditions in the chamber: simulation of temporary malfunction of different elements of the life support system (LSS). During this time, the temperature in the pressure chamber was raised to 32°C and humidity to 87%, with concurrent increase in CO_2 content to 3% [2].

The 1st to 3d series of studies lasted 30 days each.

In the 4th series, the studies lasted 90 days and CO concentration constituted 10 mg/m^3. However, in simulating malfunction of the LSS, in addition to raising ambient temperature (to 35°C), CO_2 concentration (to 3%) and humidity (to 90%), the CO level was raised to 46 mg/m^3.

For evaluation of glucocorticoid function of the adrenal cortex, we assayed 11-oxycorticoids (11-OC) in blood plasma by the fluorimetric method of Yu. A. Pankov and I. Ya. Usvatova [11].

Mineralocorticoid function of the adrenal cortex was evaluated by the levels of sodium and potassium in erythrocytes, since one can make an indirect judgment about the level of aldosterone production on the basis of concentration of these elements [12, 13]. Potassium and sodium content of erythrocytes was assayed by a unified method using an FPF-58 instrument [14].

The obtained data were submitted to processing by the method of variation statistics.

Results and Discussion

We observed an increase ($P<0.01$) in 11-OC concentration in blood plasma on the 5th day of exposure to CO in a cocnentration of 20 mg/m^3 (1st series of studies). On the 19th day, 11-OC content dropped to the initial level.

Thereafter (16th, 22d and 28th days), there was an increase in 11-OC content of plasma, the maximum rise being observed on the 28th day ($P<0.01$). After the tests, the concentration of plasma 11-OC was below the background level (see Table).

11-OC content (μg%) in plasma; potassium and sodium content (meq/ℓ) in blood erythrocytes of subjects kept in a pressure chamber with elevated CO content (M±m)

Substance examined	Series	Background period	Experimental period, days					Recovery period
			4	10	16	22	28	
11-OC	1	29.0 ± 1.07	36.8 ± 1.18	29.9 ± 3.6	32.2 ± 3.4	35.0 ± 1.9	36.6 ± 1.9	25.0 ± 1.72
	2	26.0 ± 1.8	32.2 ± 2.1	38.1 ± 2.7	22.4 ± 2.9	45.1 ± 0.9	29.4 ± 4.02	27.0 ± 1.03
	3	26.5 ± 0.7	39.0 ± 3.3	27.7 ± 0.7	30.2 ± 2.4	38.0 ± 3.5	40.4 ± 4.7	36.1 ± 2.0
K	1	83.8 ± 1.35	90.5 ± 2.95	98.8 ± 2.2	95.7 ± 1.6	95.5 ± 1.7	100.8 ± 6.5	90.1 ± 2.9
	2	91.2 ± 2.75	87.6 ± 4.75	95.1 ± 1.2	94.1 ± 0.83	98.1 ± 0.82	85.6 ± 5.65	81.1 ± 6.6
	3	92.9 ± 0.67	78.6 ± 2.69	78.7 ± 7.31	—	91.6 ± 3.96	—	91.3 ± 1.48
Na	1	18.3 ± 0.91	17.8 ± 0.98	16.4 ± 0.72	14.8 ± 1.1	14.9 ± 0.96	14.6 ± 0.41	17.8 ± 1.22
	2	15.0 ± 0.9	14.6 ± 0.6	15.1 ± 0.7	13.9 ± 0.7	17.2 ± 0.8	15.5 ± 1.7	18.8 ± 0.4
	3	12.5 ± 0.55	15.9 ± 1.3	13.7 ± 0.5	—	13.1 ± 0.5	—	15.8 ± 0.6

Potassium content of erythrocytes was above the base level (particularly on the 19th and 28th days). There was a tendency toward normalization of erythrocyte potassium content in the recovery period. The concentration of sodium in erythrocytes was below the base levels at all tested times.

In the 2d series of tests (CO concentration 15 mg/m^3) the subjects presented elevation of blood plasma 11-OC level on the 4th and 10th days. On the 16th day, there was a decrease in 11-OC content. A second, significant increase in 11-OC concentration ($P<0.01$) was demonstrated on the 22d day (see Table). There was little difference from base levels in potassium and sodium content of erythrocytes throughout the test period (see Table).

The results of examining blood plasma 11-OC in the 3d series of studies (CO concentration 15 mg/m^3) revealed that the dynamics of changes in blood 11-OC content were similar to those in the 1st series of tests. After completion of the study, the concentration of 11-OC remained high ($P<0.05$) (see Table). Potassium content of erythrocytes was low on the 4th ($P<0.01$) and 10th ($P<0.01$) days of the test (see Table). A slight elevation of sodium level in erythrocytes was noted on the 4th day and in the recovery period (see Table).

The data obtained in the course of the 4th series of tests revealed that, against the background of simulated temporary malfunction of the LSS, on the 21st day of the test the subjects presented an increase in blood plasma 11-OC level (37.1±2.45 μg%, versus 31.5±0.59 μg% in the background period). There was another slight increase in plasma 11-OC (35.4±1.21 μg%) prior to the end of the study (on the 90th day).

In those cases where normal microclimate conditions were maintained in the pressure chamber with CO level of 10 mg/m^3, 11-OC content of plasma fluctuated over the background range on the 64th and 81st days of the test (29.1±3.66 and 30.8±4.7 μg%, respectively). On the 71st day, plasma 11-OC content was somewhat decreased (to 24.6±2.9 μg%).

The results of our studies indicate that a concentration of 10 mg/m^3 CO (4th series) did not affect blood plasma 11-OC content in our subjects, whereas in a concentration of 15 and 20 mg/m^3 this parameter increased at certain times, which could be interpreted as increased activity of adaptation mechanisms under such conditions. The activity of adaptation processes also increased with combined exposure to CO, CO_2, elevated temperature and increased humidity. This was associated with increase in glucocorticoid function of the adrenal cortex, whereas mineralocorticoid function showed virtually no change. It is known [2] that an increased CO level in inhaled air leads to an increase in blood carboxyhemoglobin content. This, in turn, induces tissular hypoxia [3, 4]. It was shown [6] that adrenocortical hormones, particularly glucocorticoids, enhance nonspecific resistance of the body in the presence of hypoxia and, consequently, they are involved in the process of adaptation to unusual living conditions in a pressure chamber with high CO content.

Thus, the results of our studies revealed that the body adapted to the environment of a pressure chamber with the active participation of the adrenal cortex. The degree and direction of changes were related to the concentration of CO in the pressure chamber.

BIBLIOGRAPHY

1. Sjostrand, T. ANN. N.Y. ACAD. SCI., Vol 174, 1970, p 1.

2. Savina, V. P.; Sokolov, N. L.; and Nikitin, Ye. I. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1976, p 62.

3. Vasil'yev, G. A.: Medvedev, Yu. A.; and Khmel'nitskiy, O. K. "The Endocrine System in the Presence of Hypoxia," Leningrad, 1974.

4. Tiunov, L. A., and Kustov, V. V. "Toxicology of Carbon Monoxide," Leningrad, 1969.

5. Shtabskiy, B. M. VRACH. DELO [Medical Record], No 7, 1961, p 101.

6. Pukhov, V. A. "Pathogenesis, Complex Prevention and Treatment of Hypoxia," author abstract of candidatorial dissertation, Leningrad, 1964.

7. Berka, I.; Kadlec, K.; Novotny, S.; et al. PRACOV. LEK., Vol 8, 1956, p 4.

8. Fimiani, R., and Castellino, N. FOLIA MED. (Naples). Vol 41, 1958, p 454.

9. Peysakhovich, I. M. in "Industrial Toxic Agents," Khar'kov, 1928, p 147.

10. Agadzhanyan, N. A., and Sergiyenko, A. V. DOKL. AN SSSR, SER. BIOL. [Reports of the USSR Academy of Sciences, Biology Series], Vol 191, No 2, 1970, p 487.

11. Pankov, Yu. A., and Usvatova, I. Ya. in "Metody klinicheskoy biokhimii gormonov i mediatorov" [Methods in Clinical Biochemistry of Hormones and Mediators] by V. V. Men'shikov, Moscow, 1966, p 29.

12. Men'shikov, V. V. Ibid, 2d ed., Moscow, 1969, p 145.

13. Frenkel', I. D. "Neurohumoral Mechanisms of Regulation in Patients Suffering From Rheumatoid Polyarthritis and Peptic Ulcer Treated With Physical Factors," author abstract of doctoral dissertation, Moscow, 1971.

14. Mikhaylova, S. P. in "Unifitsirovannyye metody klinicheskikh laboratornykh issledovaniy" [Standardized Methods for Clinical Laboratory Tests], Moscow, Vyp 6, 1974, p 77.

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EFFECT OF HYPOXIA AND HYPERCAPNIA ON LACTATE AND PYRUVATE LEVELS IN RAT BLOOD AND MYOCARDIUM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1980 pp 80-82

[Article by N. I. Mikhalkina, submitted 26 Sep 77]

[Text] We know from the literature that activation of the process of glycolysis is observed in the heart in the presence of hypoxia, which develops in the presence of diseases of the cardiovascular and respiratory systems [1-3], significant muscular loads [4-6], as well as altitude hypoxia [7-9]. Such factors as increased production of lactic acid (LA) [2] and change in level of pyruvic acid (PA), from which LA is formed as a result of oxidoreduction with $NAD \cdot H_2$, are indicative of intensification of glycolytic processes.

There is a significant number of works dealing with the study of activation of anaerobic processes in the presence of hypoxia [1, 2, 5, 7]. There is information to the effect that the combined action of hypoxia and hypercapnia is more effective than their separate effects [10], and that the former enhances body resistance to acute hypoxia and other stress factors [11]. This is related to the fact that carbon dioxide has the capacity to lower tissular oxygen requirements, diminish affinity of oxygen for hemoglobin and thereby causes oxygen to pass from blood into tissues [11]. There are also data indicative of the role of the hypercapnic stimulus in the control of pulmonary ventilation and stimulation of chemoreceptors [10, 12]. Data have been obtained that indicate an increase in delivery of blood to the myocardium and stimulation of compensatory and adaptive changes in the coronary circulation as a result of the use of hypoxic and hypercapnic loads [13].

Our objective here was to study the dynamics of LA and PA during recurrent brief exposure of rats to hypoxia and hypercapnia.

Methods

Experiments were conducted on rats weighing 160-250 g. To obtain the effect of the hypoxic-hypercapnic factor, the animals were kept in an unventilated place for about 1.5 h daily (2 rats per 7.6 ℓ desiccator) until they developed overt signs of hypoxia. The oxygen content in the closed compartment at the end of the exposure period constituted 6.8±0.03% and that of carbon dioxide 8.8±0.03%. Experiments were conducted on 7 groups of rats, which were sacrificed with chloral hydrate (2 g/kg) after 1, 2, 3, 7, 10, 15 and 30 days of exposure to hypoxia and hypercapnia. The eighth group served as a control. We assayed LA in blood and tissue of the left and right heart according to Barker and Summerson, PA by the Natelson method (in milligram percent per 100 mg tissue or 100 μℓ blood). In analyzing the material, we used the estimated value of LA/PA, which is also an indicator of intensity of anaerobic processes in the opinion of a number of researchers [3, 6, 9, 14, 15].

The data were submitted to statistical processing according to I. A. Oyvin [16].

Results and Discussion

The data in Tables 1 and 2 show that already single exposure to the hypoxic-hypercapnic factor induced changes in lactate and pyruvate concentrations in all specimens examined. These changes were more significant in the blood and tissue of the left heart. For example, in left heart blood, LA content increased by 164% ($P<0.001$) and PA by 418% ($P<0.05$). LA/PA had the highest value in left heart tissue (310%; $P<0.02$).

We observed further increase in lactate (to 298% in right heart tissue; $P<0.001$) and pyruvate (by 508% in blood of left heart; $P<0.05$), with the exception of a few specimens, on the 2d, 3d and 7th days. LA/PA levels were very high (1233 mg% in left heart tissue; $P<0.01$).

By the 19th day, there was an increase in concentration of LA and PA, and PA reached a maximum (the increase constituted 525% in left heart blood; $P<0.001$). In view of the more marked increase in concentration of PA at this time there was a decline of LA/PA.

By the 15th and 30th days we observed a decline in lactate level, although it still remained somewhat above control values. There was a drastic drop in pyruvate level, for which reason LA/PA remained very high.

In analyzing the obtained data, it must be noted that there was accumulation of lactate in all of the experiments. At the early stages of exposure to hypoxia and hypercapnia, this accumulation of LA proceeded with concurrent increase in PA, whereas at the later stages not only did the PA level fail to rise, it even dropped. This is consistent with data in the literature pertaining to two types of metabolic acidosis [14, 17].

Table 1. Levels of LA, PA and LA/PA with repeated exposure to hypoxia and hypercapnia (mg%/100 mg tissue or 100 μℓ blood) [C--control]

Exposure time, days	n	Right heart tissue			Left heart tissue			Right heart blood			Left heart blood		
		LA	PA	LA/PA	LA	PA	LA/PA	LA	PA	LA/PA	LA	PA	LA/PA
C	7	113,00 ± 21,65	0,538±0,30	210,03 ± 125,50	135,87 ± 13,53	1,162±0,503	116,92±83,3	122,3 ± 46,56	1,589±0,56	76,96±49,76	125,25 ± 14,26	0,627±0,61	199,70±75,65
1 P	6	136,50 ± 15,93 >0,2	0,981±0,24 >0,2	277,03 ± 73,00 >0,5	201,00 ± 18,30 <0,002	0,289±0,06 >0,1	363,16±43,7 <0,02	153,33 ± 15,42 >0,5	1,630±0,29 >0,5	135,95±44,50 >0,2	205,50 ± 31,17 <0,001	2,622±0,655 <0,05	146,27±52,04 >C,2
2 P	6	335,00 ± 41,87 <0,001	0,262±0,018 >0,5	761,33 ± 81,25 <0,01	295,00 ± 48,64 <0,001	0,166±0,004 <0,05	2016,48±250,00 <0,001	295 ± 42,58 <0,02	1,475±0,434 >0,5	370,18±147,9 >0,1	209,00 ± 24,47 <0,02	2,911±0,53 <0,02	85,86±11,41 >0,2
3 P	6	322,00 ± 90,00 <0,05	0,788±0,23 >0,5	493,68 ± 128,18 >0,1	179,00 ± 20,92 >0,1	1,730±1,15 >0,5	862,93±338,75 <0,05	167,40 ± 49,32 >0,2	1,978±0,18 >0,2	92,15±19,70 >0,5	188,00 ± 21,13 <0,05	2,378±0,761 <0,05	79,05±39,70 >0,2
7 P	6	331,10 ± 85,6 <0,05	0,873±0,57 >0,5	379,6 ± 65,0 >0,2	375,00 ± 96,81 <0,05	0,304±0,13 >0,1	1233,55±279,00 <0,01	219,20 ± 51,34 >0,1	1,441±0,219 >0,5	169,89±27,2 >0,1	219,60 ± 32,22 <0,02	3,189±0,81 <0,05	109,18±40,40 >0,1
10 P	6	478,00 ± 61,67 <0,001	2,332±0,46 <0,01	241,50 ± 60,13 >0,5	331,00 ± 32,03 <0,001	1,999±0,32 >0,1	350,86±115,86 >0,2	378,00 ± 112,28 <0,001	4,885±0,32 <0,001	88,37±15,66 >0,5	266,00 ± 41,80 <0,02	3,297±0,81 <0,001	77,05±12,81 >0,1
15 P	6	132,50 ± 10,97 >0,2	0,291±0,057 >0,5	751,77 ± 418,80 >0,2	107,00 ± 31,54 >0,2	0,221±0,015 >0,1	1149,8±237,10 <0,001	141,75 ± 1,95 >0,2	0,256±0,073 <0,05	441,3±70,90 <0,001	105,92 ± 3,66 >0,2	0,717±0,091 >0,2	161,26±39,93 >0,5
30 P	10	181,33 ± 20,88 <0,02	0,271±0,06 >0,2	1099,00 ± 254,20 <0,01	202,80 ± 37,51 >0,01	0,376±0,081 >0,01	981,31±909,30 <0,02	165,00 ± 25,26 >0,05	1,031±0,15 >0,02	237,73±47,70 <0,02	172,80 ± 16,22 <0,05	2,148±0,315 <0,05	92,57±18,20 >0,2

Table 2. Changes in LA, PA and LA/PA with repeated exposure to hypoxia and hypercapnia (%)

Exposure time, days	Right heart tissue			Left heart tissue			Right heart blood			Left heart blood		
	LA	PA	LA/PA	LA	PA	LA/PA	LA	PA	LA/PA	LA	PA	LA/PA
1	120,79	182,34	131,90	147,93	24,87	310,60	125,37	102,58	176,61	164,07	418,18	73,22
2	296,46	48,69	362,48	217,11	14,28	1749,91	241,21	109,81	481,00	166,86	464,27	42,98
3	284,95	146,46	235,05	131,74	149,39	738,05	136,87	124,48	119,69	150,09	379,26	39,57
7	293,27	162,26	180,73	275,99	26,16	1055,03	203,76	90,68	220,75	175,32	508,61	54,65
10	423,00	433,45	114,98	243,61	172,03	300,08	309,07	307,42	114,82	212,37	525,83	38,57
15	117,25	54,64	357,93	122,91	19,01	983,40	118,35	16,11	573,41	84,56	114,35	80,27
30	160,46	50,37	523,25	149,26	32,35	839,30	134,91	65,07	308,90	137,96	342,58	46,34

Single exposure to hypoxia combined with hypercapnia induced the maximum changes in LA and PA concentration in the left heart. Further exposure to these factors led to even more significant changes in levels of the recorded products of glycolysis, particularly lactate in the right heart. Evidently, this depended on the part of the heart that was subject to the greater functional load at any given period of the experiment. Thus, under hypoxic conditions the degree of activation of nucleic acid and protein synthesis was much more marked in the right ventricle than the left [18].

There are some difficulties involved in interpreting the low level of PA, which was observed in the experiments by the 15th and 30th days of exposure to hypoxia and hypercapnia. According to the literature, this could be related either to intensification of anaerobic glycolysis [3, 6, 8], as indicated by the high values for LA/PA, or intensification of aerobic processes through which pyruvate is involved in other elements of biochemical processes. Additional studies must be conducted to answer this question.

Thus, there are changes in glycolytic metabolism in the rat heart under the influence of hypoxia and hypercapnia.

BIBLIOGRAPHY

1. Tatarkin, V. M. "Activity of Lactate Dehydrogenase, Levels of Lactic and Pyruvic Acids in Blood in the Presence of Circulatory Insufficiency," candidatorial dissertation, Moscow, 1966.

2. Vollenberger, A., and Krauze, Ye. G. in "Korrelyatsiya krovosnabzheniya s metabolizmom i funktsiyey" [Correlation between Delivery of Blood, Metabolism and Function], Tbilisi, 1969, pp 271-287.

3. Bulanova, O. N., and Zaks, I. O. PAT. FIZIOL. [Pathological Physiology], No 1, 1973, pp 51-53.

4. Nemirovich-Danchenko, O. R. in "Vsesoyuznaya nauch. konf. po fiziologii, morfologii, biokhimii i biomekhanike myshechnoy deyatel'nosti. 9-ya. Materialy" [Proceedings of 9th All-Union Scientific Conference on Physiology, Morphology, Biochemistry and Biomechanics of Muscular Activity], Moscow, Vol 4, 1966, pp 64-65.

5. Razumovskiy, Ye. A. in "Vsesoyuznaya konf. po fiziologii, morfologii, biomekhanike i biokhimii myshechnoy deyatel'nosti. 11-ya. Materialy" [Proceedings of 11th All-Union Conference on Physiology, Morphology, Biomechanics and Biochemistry of Muscular Activity], Sverdlovsk, 1970, p 344.

6. Brodan, V., and Kun, E. CHEKHOSLOV. MED. OBOZR. [Czech Medical Review], Vol 17, No 2, 1971, pp 93-115.

7. Nazarenko, A. I. FIZIOL. ZH. [Physiological Journal (Ukrainian)], No 3, 1975, pp 377-380.

8. Barbashova, Z. I. "Acclimatization to Hypoxia and Physiological Mechanisms Thereof," Moscow--Leningrad, 1960.

9. Dudchenko, A. M. in "Mitokhondrii" [Mitochondria], Moscow, 1976, pp 177-182.

10. Breslav, I. S. "Voluntary Control of Breathing in Man," Leningrad, 1975.

11. Marshak, M. Ye. "Physiological Significance of Carbon Dioxide," Moscow, 1969.

12. Agadzhanyan, N. A.; Davydov, G. A.; and Spasskiy, Yu. A. FIZIOLOGIYA CHELOVEKA [Human Physiology], Vol 3, No 2, 1977, pp 343-354.

13. Zver'kova, Ye. Ye. IZV. AN KAZAKHSK. SSR. SER. BIOL. [News of the Kazakh Academy of Sciences, Biology Series], No 1, 1977, pp 80-83.

14. Perevoshchikova, Ye. P. PEDIATRIYA [Pediatrics], No 7, 1972, pp 69-72.

15. Neil, W. A., et al. AM. J. PHYSIOL., Vol 204, 1963, pp 427-433.

16. Oyvin, I. A. PAT. FIZIOL., No 4, 1960, pp 76-85.

17. Huckabee, W. J. CLIN. INVEST., Vol 37, 1958, p 244.

18. Meyerson, F. Z.; Mayzelis, M. Ya.; and Malkin, V. B. in "Dostizheniya sovremennoy kardiologii" [Advances in Modern Cardiology], Moscow, 1970, pp 277-288.

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STUDY OF RADIOPROTECTIVE EFFECT OF HIGH-INTENSITY MAGNETIC FIELDS ON MAMMALIAN CELL CULTURES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 1, 1980 pp 83-84

[Article by Z. Ye. Vnukova, submitted 16 Jan 78]

[Text] Plans for magnetic protection [1, 2] against ionizing radiation served as the grounds for conducting experiments, the objective of which was to study the combined effect of ionizing radiation and stationary magnetic fields (SMF) on various biological objects [3-8]. There was improvement of hematological parameters and a higher animal survival rate with a certain combination of these factors [9-11]. Very few such experiments were conducted on unicellular organisms and cell cultures, and their findings were far from the same [12, 13].

We submit here the results of experiments used to study the 1000 Oe SMF on the effect of gamma radiation on a mammalian cell culture in vitro.

Methods

In this study, we used two cell cultures: fibroblasts of mice (cell line L) and Chinese hamsters (subline 237). The cells were cultured in medium 199 (L cells) and Eagle's medium (Chinese hamster cells) with 10% bovine serum and antibiotics at a temperature of 36.5°C. The radiation effect was evaluated according to rate of restoration of cell division, level of chromosomal aberrations in the first postradiation mitosis and cell survival. The cultures were exposed to radiation from a ^{137}Cs source, in doses of 200 and 400 R, at a dose rate of 38 R/min. To determine the percentage of chromosomal aberrations, we exposed 2-day cultures to radiation, without exposure to SMF (control) and with exposure to 1000 Oe SMF for 2 days, as well as cells after 6-day culturing in SMF (4 days of the first passage and 2 days of the second), then fixed them 8 h after irradiation.

We used the method of Puck [14] to determine cell survival. The cells were fixed after 10 days of cultivation, and they were divided into two equal parts: one irradiated culture was exposed to the SMF and the other was not.

The radiation technique has been described elsewhere [15].

Results and Discussion

There was no change in rate of restoration of cell division 6 h after exposure to radiation in a dosage of 400 R and SMF. There was also no difference between intact Chinese hamster cells and those exposed to SMF with respect to level of chromosomal aberrations (see Table).

Chromosomal aberrations in Chinese hamster cells (%) (M±m)

Exposure to	200 R	400 R	Intact cells
GMP			5,2 ± 0,48
SMF			4,8 ± 0,43
GMP-R-GMP	12,2±1,38	20,4 ± 1,60	
GMP-R-SMF	12,3±1,52	20,9 ± 1,74	
SMF-R-GMP	11,5±1,28	19,6 ± 1,70	
SMF-R-SMF	14,2±0,85	21,5 ± 1,55	

Key: R) radiation
SMF) stationary magnetic field
GMP) expansion not known*

The survival of L cells exposed to GMP* constituted 40.4±2.02% after exposure to radiation in a dose of 200 R and 9.7±1.42% after a dose of 400 R; the figures were 42.2±4.43 and 12.5±1.25%, respectively, with exposure to SMF. The differences are statistically insignificant. Long-term exposure of growing cultures to SMF also failed to alter cell survival: the survival rate was 28.3±5.11% after 4-day culturing of L cells in SMF and irradiation in a dosage of 400 R, versus 30.7±3.8% in the control (SMF alone).

These studies revealed that exposure of mammalian cells in vitro to SMF before or after irradiation from a source of gamma radiation did not alter either the rate of restoration of cell division or the number of chromosomal breaks demonstrated in the first postradiation mitosis. Different combinations of 1000 Oe SMF and ionizing radiation did not change the survival rate for irradiated cells.

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*Translator's note: GMP appears more than once in this article; MP probably refers to magnetic fields, but meaning of G is not clear.

Similar results were obtained by other researchers [16]. The increase in survival rate of animals exposed to radiation after SMF, which was reported by Barnothy [6, 7] and Shein [11], may be related to some systemic functional changes developing under the influence of SMF.

BIBLIOGRAPHY

1. Trukhanov, K. A.; Ryabova, T. Ya.; and Morozov, D. Kh. "Active Protection of Spacecraft," Moscow, 1970.

2. Busby, D. E. SPACE LIFE SCI., Vol 1, 1968, pp 23-63.

3. Galaktionova, G. V., and Strzhizhovskiy, A. D. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1974, pp 25-28.

4. Pozolotin, A. A. in "Voprosy gematologii, radiobiologii i biologicheskogo deystviya magnitnykh poley" [Problems of Hematology, Radiobiology and Biological Effects of Magnetic Fields], Tomsk, 1965, pp 332-335.

5. Idem, in "Vliyaniye magnitnykh poley na biologicheskiye ob"yekty" [Effects of Magnetic Fields on Biological Objects], Moscow, 1971, pp 186-187.

6. Barnothy, M. F. NATURE, Vol 200, 1963, pp 279-286.

7. Idem, in "Biological Effects of Magnetic Fields," New York, Vol 1, 1964, pp 127-131.

8. Barnothy, M. F., and Barnothy, J. M. NATURE, Vol 181, 1958, pp 1785-1786.

9. Abdullayev, M. D., and Zhdanova, S. M. in "Vliyaniye iskusstvennykh magnitnykh poley na zhivyye organizmy. Vsesoyuznyy simpozium. Materialy" [Proceedings of All-Union Symposium on the Effects of Artificial Magnetic Fields on Living Organisms], Baku, 1972, pp 7-9.

10. Savchenko, N. Ya.; Shein, V. I.; and Grigor'yev, Yu. G. in "Magnitnoye pole v meditsine" [Magnetic Fields in Medicine], Frunze, 1974, pp 116-117.

11. Shein, V. I. in "Vliyaniye magnitnykh poley na biologicheskiye ob"yekty. Vsesoyuznyy simpozium. 3-y. Materialy" [Proceedings of 3d All-Union Symposium on Effects of Magnetic Fields on Biological Objects], Kaliningrad, 1975, pp 223-224.

12. Vlasov, A. Ye. Ibid, pp 72-73.

13. Sosunov, A. V., and Tripuzov, A. N. "Issledovaniya po geomagnetizmu, aeronomii i fizike solntsa" [Studies of Geomagnetism, Aeronomy and Solar Physics], Vyp 17, 1971, p 137.

14. Puck, T. T. in "Biophysical Science," New York, 1959, pp 433-448.

15. Sushkov, F. V., and Neyman, O. V. in "Vliyaniye iskusstvennykh magnitnykh poley na zhivyye organizmy. Vsesoyuznyy simpozium. Materialy," Baku, 1972, pp 125-127.

16. Katola, V. M.; Chertov, A. D.; and Gordiyenko, V. P. in "Vliyaniye yestestvennykh i slabykh iskusstvennykh magnitnykh poley na biologicheskiye ob"yekty" [Effects of Natural and Weak Artificial Magnetic Fields on Biological Objects], Belgorod, 1973, pp 69-71.

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STUDIES OF THE EFFECTS OF STATIONARY MAGNETIC FIELDS ON RAT ERYTHRON

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 1, 1980 pp 84-87

[Article by A. D. Pavlov, A. I. Solov'yev, Yu. D. Goncharenko and
Ye. N. Pashukov, submitted 26 Oct 78]

[Text] There are few data in the literature concerning functional changes in erythron under the influence of stationary magnetic fields (SMF), and they are contradictory [1-4]. For this reason, our objective here was to study the dynamics of erythropoiesis and erythropoietic activity of serum in rats exposed to 1000 Oe SMF.

Methods

Experiments were conducted on 187 mongrel male rats weighing 160-220 g and 122 female $(CBA \times C57Bl)F_1$ mice weighing 16-22 g. The animals were put in the SMF in plexiglas containers; the temperature, humidity and light were kept constant. They were exposed at the same time of day. The gradient of field intensity did not exceed 4% and pulsation of the variable component (100 Hz) did not exceed 0.05%. The working space between the poles constituted 120 mm and the area was 240×260 mm.

In the first series of experiments we tested the biological effect of 1000 Oe SMF with 3-h exposure and in the second, with 24-h exposure. We assayed erythrocytes, reticulocytes, hemoglobin and hematocrit immediately and 1, 3 and 10 days after exposure. We determined erythropoietic activity at the same times. In a separate series of experiments, we studied the life span of erythrocytes during exposure to SMF.

Erythropoietin titer in serum samples, expressed in international units (IU) of standard B, was assayed by the percentage of incorporation of ^{59}Fe in erythrocytes of polycythemic mice. To induce polycythemia, the mice were kept at an "altitude" of 6000 m for 18 h/day, for 21 days. We used a standard erythropoietin preparation to plot the dose-effect curve. The standard was injected intraperitoneally in doses of 0.1, 0.2, 0.5 and 1.0 IU in two portions, in a volume of 0.5 mℓ, on the 3d and 4th posthypoxia days. Sterile saline with addition of 0.1% albumin was used as diluent. On the 6th day, the animals were given intraperitoneal injections of 1.0 μCi ^{59}Fe in 0.5 m saline. The mice were sacrificed after 24 h to assay hematocrit and radioactivity of blood samples, which was determined in 0.2 mℓ samples with a scintillation well-counter. We counted the incorporation of ^{59}Fe in erythrocytes on the basis of total blood volume, which constituted 6% of body weight. The effect as a function of dosage was plotted on the basis of four points (Figure 1). In our experiments, we used a testing system that is a modification of the method of Cotes [5].

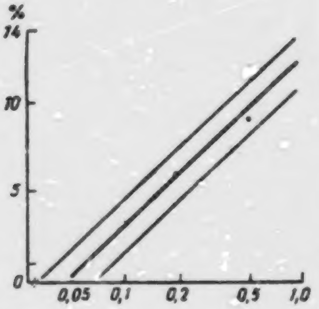

Figure 1.
Erythropoietic reaction as a function of dosage in a semilogarithmic system of coordinates.

X-axis, IU; y-axis, % uptake of ^{59}Fe in erythrocytes of posthypoxic polycythemic mice; b = 9.23, SD = ±1.436, index of precision SD/b = 0.155

The life span of erythrocytes was determined in 19 female Wistar rats with the use of ^{51}Cr. A solution of $Na_2{}^{51}CrO_4$ was injected intraperitoneally at the rate of 7 μCi/100 g weight. Concurrently, $Na_2{}^{51}CrO_4$ was injected in control rats. We took blood samples twice, in a volume of 0.1 mℓ, from the caudal vein after 1, 3, 6 and 9 days. Radioactivity was determined on an USD-1 with a scintillation counter. Samples taken 24 h after injection of ^{51}Cr were considered as 100%.

Results and Discussion

There was a 74% increase in reticulocytes immediately after 3-h exposure to SMF, whereas hemoglobin, hematocrit and erythrocyte count of peripheral blood diminished unreliably (Table 1). Erythrocyte count, hemoglobin and hematocrit index remained low 1, 3 and 10 days after this exposure.

At these times, there was a 70 and 100% increase in reticulocytes, as compared to base levels (see Table 1). Immediately after 3-day exposure to SMF, erythropoietin titer in rat blood serum rose by 48%, constituting 0.089±0.012 IU (versus 0.060±0.001 IU in the control). Serum erythropoietin titer remained elevated 1, 3 and 10 days after exposure to SMF (Figure 2).

There was a decrease in hemoglobin and increease in reticulocytes by 40% in rat peripheral blood after 24-h exposure to SMF (Table 2). After 1 day, there was a decrease in erythrocyte count and hemoglobin content, while reticulocyte count remained unchanged. After 3 and 10 days, essentially the same changes persisted in hemoglobin content, erythrocyte count and hematocrit index as 1 day after exposure to SMF. However, the reticulocyte count remained 60 and 33% higher, respectively at these times. The erythropoietin titer in serum rose by 22% immediately after exposure (0.073±0.006 IU)and remained high at other tested times (see Figure 2).

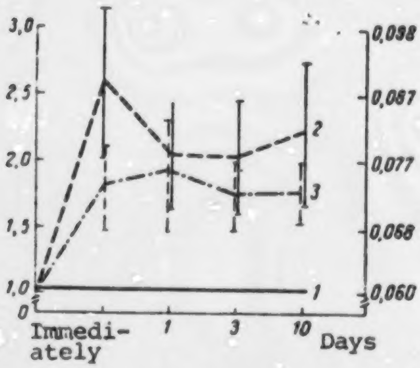

Figure 2.
Changes in erythropoietic activity of rat serum at different times after 3- and 24-h exposure to 1000 Oe SMF. X-axis, post-SMF time of examination; y-axis: % ^{59}Fe uptake in erythrocytes of posthypoxic polycythemic mice, on the left; erythropoietic titer in IU, on the right
1) control (saline with 0.1% albumin)
2,3) 3-h and 24-h exposure, respectively

Table 1. Peripheral blood indices of rats after 3-h exposure to 1000 Oe SMF

Index	Base data	Days after exposure to SMF			
		immediately	1	3	10
Erythrocytes, millions/mm^3	7.0±0,13 100,0±1.86	6,9±0,13 98,0±1,84	6.63±0,08* 90,0±1.08	6.29±0,06* 89,6±0,85	6,14±0,07* 87,7±1,0
Hemoglobin, g%	15,5±0,15 100,0±0,97	14,8±0,16* 95,6±1,03	14.3±0,15* 92,4±0,97	14,3±0,13* 92,4±0,84	14.3±0,16* 97,0±1,08
Hematocrit	46.0±0,6 100,0±1,3	44.5±0,3* 96,7±0,65	44.0±0.32* 95,6±0,7	44.0±0,32 95,6±0,7	44,6±0,25* 97,0±0,54
Reticulocytes, ‰	27,0±2,3 100,0±8,52	48,0±4.5* 174,0±16.31	46.0±3,1 170,0±11,79	51,0±6,0* 190,0±22,35	54.0±5,6* 200,0±20,74

Note: We examined 31 animals. Here and in Table 2, absolute values are given in numerator (M±m) and % of base level in the denominator. The asterisks refer to reliable differences ($P<0.05$).

The tests with ^{51}Cr revealed that the half-life of erythrothrocytes of control rats constituted 7-9 days (Figure 3). Injection of ^{51}Cr immediately after 3-h exposure to SMF failed to demonstrate any differences in reduction of radioactivity of blood samples, as compared to control rats. Somewhat faster decline of radioactivity in blood samples, as compared to control levels, was observed after 24-h exposure to SMF and administration of ^{51}Cr immediately after exposure; however, the difference was found to be statistically unreliable.

Table 2. Peripheral blood indices of rats after 24-h exposure to 1000 Oe SMF

Index	Base data	Days after exposure to SMF			
		immediately	1	3	10
Erythrocytes, millions/mm^3	7,00±0,12 100,0±1,71	6,90±0,09 98,0±1,27	6,66±0,11* 95,0±1,57	6,37±0,06* 93,0±0,87	6,45±0,48* 93,0±1,15
Hemoglobin, g%	15,0±0,16 100,0±1,06	14,5±0,15* 97,0±1,00	14,0±0,17* 93,0±1,13	14,0±0,17* 93,0±1,13	14,3±0,18* 95,0±1,2
Hematocrit	45,0±0,36 100,0±0,8	45,0±0,56 100,0±1,24	45,0±0,43 100,0±0,95	44,0±0,5 97,0±1,1	44,0±0,64 97,0±1,41
Reticulocytes, ‰	27,0±1,7 100,0±6,3	38,0±1,28* 140,0±4,71	37,0±2,6* 137,0±9,62	43,0±3,3* 160,0±12,28	35,0±1,3* 133,0±4,94

Note: A total of 32 animals was examined.

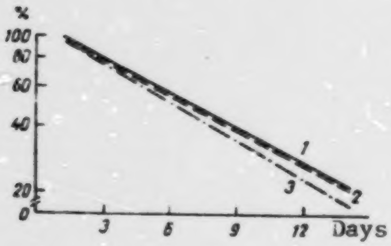

Figure 3.
Change in erythrocyte half-life (according to ^{51}Cr uptake) after 3- and 24-h exposure of rats to 1000 Oe SMF. X-axis, time of examination; y-axis, radioactivity of blood samples (% of base level)

1) control
2,3) 3- and 24-h exposure

The decrease in erythrocytes, hemoglobin and hematocrit could be attributable to at least two mechanisms: increased destruction of erythrocytes and decreased production of erythrocytes. The data indicative of slower biochemical reactions related to so-called paramagnetic molecules (hemoglobin, myoglobin, cyanocobalamin, catalase, cytochrome c and others), inhibition of active ion transport through membranes, as well as slower mitoses under the influence of SMF [6-10] are in favor of the assumption that magnetic fields have an inhibitory effect on rat erythron. The normal half-life of ^{51}Cr-labeled erythrocytes immediately after exposure to SMF does not confirm the hypothesis that there is a direct deleterious effect of 1000 Oe SMF on circulating erythrocytes. However, these data do not rule out the possibility that the "deleterious" effect of SMF on erythron cells occurs on the level of nuclear erythroid cells of bone marrow. Perhaps, this "damaged" population of erythrocytes, which begins to circulate several days after exposure to SMF, is indeed different from normal cells in structural and functional properties and has a shorter life span. If the hypothesis that there are two possible mechanisms of action of SMF is valid, the slow return to normal of all hematological indices, as well as dependence of recovery time on duration of exposure to SMF, become understandable.

The increased erythropoietic production in response to SMF indicates that there is a change in metabolism of rats exposed to this factor, and it induces an increase in O_2 requirement of tissues. Intensification of erythropoiesis in bone marrow and passage of reticulocytes into blood [11-14] should be the consequences of increased erythropoietin production. Indeed, an increase in reticulocyte content of blood was observed immediately after rats were removed from the magnetic field, and it possibly occurred during exposure to SMF.

BIBLIOGRAPHY

1. Dernov, A. I.; Senkevich, P. I.; and Lemesh, G. A. VOYEN.-MED. ZH. [Military Medical Journal], No 3, 1968, pp 43-48.

2. Nakhil'nitskaya, Z. N. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1974, pp 3-15.

3. Piruzyan, L. A.; Glezer, V. M.; Lomonosov, V. A.; et al. IZV. AN SSSR. SER. BIOL. [News of the USSR Academy of Sciences, Biology Series], No 1, 1972, pp 142-145.

4. Barnothy, J. M.; Barnothy, M. F.; and Boszormenyi-Nagy, I. NATURE, Vol 177, 1956, pp 577-578.

5. Cotes, P. M. in "Kidney Hormones," J. W. Fisher Ed., New York, 1971, pp 243-261.

6. Beischer, D. E. in "International Astronautical Congress, 12th, Proceedings," R. M. L. Baker and M. W. Makemson Ed., New York, Vol 2, 1963, pp 515-525.

7. Gross, L. in "Biological Effects of Magnetic Fields," M. F. Barnothy Ed., New York, 1964, pp 74-79.

8. Reno, V. R., and Beischer, D. E. in "Aerospace Medical Association, Annual Scientific Meeting, 37th, Abstracts," Las Vegas, 1966, pp 84-85.

9. Strzhizhovskiy, A. D., and Galaktionova, G. V. KOSMICHESKAYA BIOL., No 2, 1976, pp 63-67.

10. Barnothy, J. M. in "Biological Effects of Magnetic Fields," M. Barnothy, Ed., New York, 1964, pp 93-99.

11. Fisher, J. W.; Lajtha, L. G.; Butoo, A. S.; et al. BRIT. J. HAEMAT., Vol 11, 1965, pp 342-349.

12. Gordon, A. S., et al. in "Erythropoiesis," L. O. Jacobson and M. D. Doyle Eds., New York, 1962, pp 321-327.

13. Stohlman, V. Jr.; Brecher, G.; and Moores, R. R. Ibid, pp 162-172.

14. Joffey, J. M.; Smith, W. C.; and Wilson, R. S. SCAND. J. HAEMAT., Vol 4, 1967, pp 145-157.

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RESPIRATION AND GAS EXCHANGE UNDER HYPERBARIC CONDITIONS

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[Article by L. A. Bryantseva, I. S. Breslav and A. G. Dianov, submitted 16 Jan 78]

[English abstract from source]

The paper reviews the data available on the respiratory effects of the breathing gas increased density, which include respiratory mechanics, pulmonary ventilation, and oxygen and carbon dioxide transport. Particular attention is given to the respiratory system as a limiting factor for human performance in a hyperbaric environment. The paper discusses optimization of gas mixtures used in undersea dives.

[Text] One of the tasks confronting physiology and medicine related to exploration of the resources of the oceans is to assure not only normal vital functions but high efficiency of man while under water. This requires comprehensive studies of the effects of a hyperbaric environment on respiratory function, since high pressure and, consequently, increased density of the gas environment are factors that affect primarily respiration and exchange of gases in the body. While the maximum tolerated muscular load under ordinary conditions depends on the reserves of the circulatory system, in the case of deep dives wearing diving gear or in an underwater habitat the respiratory system plays the limiting role. S. Miles states that "physiology of respiration is the key to submarine medicine" [1].

In this survey we shall discuss current data on the effects of a hyperbaric environment on respiration and gas exchange, without touching upon such questions as the effects of high pressure neutral gases on the central nervous systems, changes in heat transfer, effects of hyperoxia, decompression disorders, etc.

Most often the effects of hyperbaric conditions are studied with the use of high pressure chambers [2-14] rather than during actual submersion (which involves methodological difficulties). Another method that has become popular more recently involves simulation of the hyperbaric factor by means of mixtures of O_2 and "heavy" gases--Ar, Xe and Sf --and the respiratory reactions to such high density mixtures turned out to be identical to the respiratory changes in a hyperbaric environment [5, 15-29]. Table 1 lists the results of our estimates, which indicate the depths that are equivalent in density to mixtures of different gases and O_2 at normal partial oxygen pressure.

Table 1. Densities of various inert gases and normoxic mixtures thereof

Parameter	Inert gases							
	N_2	H_2	He	Ne	Ar	Kr	Xe	SF_6
Gas density, g/ℓ	1,25	0,09	0,18	0,90	1,78	3,74	5,89	6,50
Relative gas density (air density is considered to be 1)	0,97	0,07	0,14	0,70	1,38	2,87	4,52	5,03
Relative density of normoxic mixture (air density taken as 1)	1,00	0,29	0,31	0,78	1,32	2,52	3,84	4,21
Depth equivalent in density to given mixture, m water column*	0	-	--	-	3	16	29	33

*Depth estimates were made with consideration of decline in fractional O_2 level required to maintain at a given depth a pO_2 of 0.21 kgf/cm^2.

The first link in the chain of changes due to high atmospheric density is an increase in resistance to gas flow in the airways. It can increase even more due to the breathing gear used in diving. S. Miles describes the sensations of a diver as follows: "You do not breathe, but suck air in, then forcefully blow it out" [1]. This factor can be simulated to some extent by using an artificial resistive (nonelastic) resistance to respiration, for example, by connecting a narrow hose or perforated diaphragm to the breathing valve [30-34]. Examination of patients with obstructive lesions to the respiratory system also yields information about the effects of increased resistance to air flow [35, 36].

As we know, resistance to gas flow in the tracheobronchial tress is attributable to the properties of inhaled gas, as well as nature and rate of flow. In a hyperbaric atmosphere, there is an increased tendency toward changing from laminar to turbulent flow. At pressures of 5-6 kgf/cm^2,* virtually all of the gas flow in the airways becomes turbulent [9, 37]. Gas density acquires decisive significance to level of resistance. Other conditions being equal, the resistance to respiration increases with increase in ambient pressure, proportionately to the square root of gas environment density [38]. At the same time, according to the equation of Rohrer, the resistance to turbulent flow is proportionate to the root of the velocity of this flow. For this reason, there is an increase in energy expended by man for the function of respiratory muscles [2, 10, 21, 31, 39] and appearance of the sensation of dyspnea [40, 41] under hyperbaric conditions.

---

*We refer here and elsewhere (unless otherwise indicated) to a normoxic nitrogen-oxygen environment.

The increase in resistance to respiration leads to slowing of maximum inspiratory and, particularly, expiratory flow in the airways [4, 41-44]. The change in magnitude of peak expiratory flow is inversely related to density of the environment or, more precisely, it is proportionate to density to the power of -0.41 or -0.45 [8, 14].

With increase in density of the environment, the magnitude of expiratory flow is limited by the following phenomenon: when intrathoracic pressure reaches a critical level during forced (due to increased resistance) expiration the small bronchi collapse. Further increase in expiratory effort becomes ineffective and can no longer cause emptying of alveolar spaces [26, 45].

In view of the limited velocities of gas flow in the airways there is a decrease in maximum breathing capacity (MBC). The change in this parameter is directly related to the increase in resistance to air flow and, consequently, inversely proportionate to the square root of gas environment density [1, 8, 26, 27, 42 and 46]. One can predict the MBC at different depths on the basis of this pattern. These estimates are listed in Table 2. It is easy to see that the decrease in MBC slows down with increase in pressure. At the same time, the MBC values are somewhat higher in actuality than the estimates [1, 43, 47]. The increased effort developed by respiratory muscles with increase in resistance to gas flow may be one explanation for this.

Indeed, increased resistance to respiration induces several reflex reactions of an adaptive nature. There is an increase in activity of respiratory motoneurons and force of contraction of respiratory muscles [33, 36, 39, 48]. Respiration becomes slower and deeper; slowing of gas flow makes it possible to overcome the resistive resistance with less expenditure of energy [5, 6, 18, 49-52].

However, these reactions compensate only partially for the effect of the increased load on the respiratory system. The observed decrease in MBC inevitably leads to limitation of efficiency [work fitness] [47, 53]. For the body cannot perform the heavy muscular work, which requires increased pulmonary ventilation in excess of the level that is the maximum under such conditions, for a long period of time. In actuality, efficiency can decrease even more in a hyperbaric atmosphere than shown by the estimates of MBC. The fact of the matter is that the maximum effort exerted by respiratory muscles leads to rapid fatigue thereof. The volume of ventilation capable of supporting man for a more or less lengthy period of time does not exceed 50% of the MBC measured in a 15-s test. Even with a maximum muscular load under hyperbaric conditions, pulmonary ventilation does not exceed 86% of MBC [42].

Table 2. Estimated MBC during respiration of normoxic (pO_2 0.21 kgf/cm^2) gas mixtures at different pressures

Pressure kgf/cm^2	Diluent gas		
	N_2	He	H_2
1	100*	175	185
5	42	100	122
10	30	77	109
20	22	56	77
30	18	48	67
50	14	37	50
100	10	26	37

*MBC at normal atmospheric pressure in an air environment is taken as 100%.

In this regard, the influence of hyperbaric conditions on overall energy expended by the body is of substantial significance. At low depths, corresponding to a 3-4-fold increase in density of the environment, there is no significant change in human gas exchange at rest or during minimal exercise [46, 54, 55]. With greater increase in density of the environment O_2 uptake and CO_2 output increase [12, 20, 21, 56]. There is a particularly noticeable increase in exchange of gases during intensive exercise performed in a hyperbaric atmosphere [10, 11, 57-61]. Most authors attribute the increase in O_2 uptake in a dense gas environment in part to an increase in function of respiratory muscles; however, the cause of this phenomenon as a whole has not yet been definitively determined.

The increase in expenditure of energy combined with decrease in functional reserves of the respiratory system under hyperbaric conditions may be manifested by inadequate pulmonary ventilation, as compared to the level of metabolic processes in the body. This leads to development of hypoxemic and hypercapnic changes, and respiratory acidosis [7, 11, 12, 26, 28, 40, 45, 47, 56-59, 62, 63]. There are some reports indicative of CO_2 retention by working divers, which resembles the findings in patients with pulmonary emphysema [54, 58, 60, 64-66].

It has been empirically established that the ratio of respiratory function to external work performed by man should not exceed 1.6% and, in the case of prolonged physical exercise, 0.25% [67]. We can make the following estimate on the basis of this rule. Let assume that a diver must perform work of 50 W at a depth of 100 m. This load requires an increase in pulmonary ventilation to 20-25 ℓ/min. Considering the density of the environment (but not the resistance generated by the breathing equipment), the work of the respiratory muscles will constitute about 0.5 W, i.e., 1% of the useful load. Consequently, man will be able to work for only a short time under such conditions.

On the basis of the results of studies and estimates, some authors concluded that man is capable of performing heavy work (about 200 W) for a short time and moderate work (100 W) for a long time even when there is a 20-fold increase in density of the respiratory environment, as compared to the air at sea level [47]. However, most researchers propose a significantly lower maximum density of the atmosphere: about 9-fold for a moderate load (110-125 W) and 6-fold for submaximum (150-200) brief load [7, 14, 26]. When working in a denser environment, there is development of dyspnea and CO_2 retention in the body [26, 40, 68].

Disturbances in pulmonary exchange of gases under hyperbaric conditions could be attributable not only to the influence of increased resistance to gas flow on the mechanics of the respiratory act. In this case, the changes in alveolar-arterial gradients of respiratory gases (a-Ap_{CO_2} and A-ap_{O_2}), which reflect loss of O_2 and CO_2 tension when passing from the lungs into blood and back, acquire substantial significance. These losses consist of several components, including intraalveolar diffusion of gases, diffusion thereof through the alveolocapillary membrane and presence of an anatomical or physiological arteriovenous shunt. Mathematical analysis of the behavior of each of these components predicts the increase in O_2 and CO_2 gradients in a high density environment [69]. This conforms with Graham's law, according to which the rate of gas diffusion, other conditions being equal, is inversely proportionate to the square root of the density of the gas in question.

However, the results of studies pertaining to A-ap_{O_2} and a-Ap_{CO_2} under hyperbaric conditions are not always by far consistent with such a conclusion. In experiments on anesthetized and artificially ventilated dogs, it was shown that A-ap_{O_2} by no means increases with increase in density of the respiratory environment. In one of these studies [66], breathing gas mixtures varying in density (He-O_2, N_2-O_2, SF_6-O_2) did not affect this gradient, whereas in the case of an SF_6-O_2 mixture combined with pressure elevation to 4 kgf/cm^2 it even decreased. In another study [29], a decrease in a-Ap_{CO_2} was obtained when breathing a dense mixture at normal pressure. The gradient was at a maximum when using an He-O_2 mixture (20.0±3.7), lowest with SF_6-O_2 (14.2±2.6) and between these two when breathing air (16.9±3.2 mm Hg). At the same time, analysis of the results of these studies did not confirm the "increase in efficiency of respiration" in denser gas environments as postulated by the authors: arterial pO_2 when breathing various normoxic mixtures (with He, N_2 and SF_6) was virtually the same (83.7±3.5, 82.8±1.5 and 84.7±2.9 mm Hg, respectively).

Studies of alveoloarterial gradients of respiratory gases in man using respiratory environments varying in density also failed to yield unequivocal results. Thus, virtually the same levels of A-apO_2 were observed with mixtures of He-O_2 and Ar-O_2; however, they were considerably higher than when breathing air [70]. Some increase in A-apO_2 was noted at a pressure of 41 kgf/cm^2 [55]. Some authors believe that this gradient declines due to increase in pO_2 of arterial blood when breathing dense mixtures (Ar-O_2, SF_6-O_2) [19, 44].

In a significant number of the cited works, no consistent influence of density of the gas environment on a-Ap_{CO_2} was demonstrable.

In the opinion of most researchers, the changes in A-ap_{O_2} in a dense environment occur due to change in nonuniformity of layered distribution of gas in the lungs, as well as ventilation-perfusion ratios [19, 22, 23, 25, 69, 71, 72]. For this reason, there is also a change in physiological dead space: it is greater when inhaling denser mixtures (for example, SF_6-O_2) than with less dense mixtures (He-O_2) [71, 73-75]. Evidently, the influence of density of respiratory mixture, which affects intrapulmonary diffusion, has little effect on the membrane component of the alveoloarterial gradient. This is indicated by the lack of relationship between diffusion capacity of the lungs and density of the environment; it was demonstrated in several studies, in which this parameter was determined by means of CO (DL_{CO}), that it is about the same when breathing mixtures of O_2 with He, Ar and SF_6 [23, 29]. True, in one such study [75], an increase in DL_{CO} was demonstrated with increase in density of diluent gas, but this finding was attributed in part to the influence of this factor on alveolar ventilation.

As we know, O_2 and CO_2 tension in arterial blood and tissues is the most important criterion of the effect of any factor on transport of respiratory gases in the body. The studies of Chouteau et al. [62, 76] demonstrated that disorders developed in experimental animals (goats), the cause of which the researchers considered to be hypoxemia, with increase in density of the environment by means of raising overall pressure (with retention of normal pO_2) or with a combination of high pressure and the use of an Ar-O_2 mixture. Indeed, elevation of pO_2 in the chamber atmosphere eliminated this phenomenon. Subsequent readings of arterial pO_2 in rabbits confirmed the decrease in blood oxygenation under hyperbaric conditions [77]. It was reported that there was a decrease in amount of oxygen transported by blood per minute in aquanauts, even when they submerged to small depths [78, 79].

In cats exposed to hyperbaric conditions, pO_2 in cerebrocortical tissue decreased while pCO_2 increased with increase in density of the environment (mixtures of He, N and Ar were used) [80]. True, pO_2 of the brain did not drop in dogs inhaling a mixture of He and O_2 at a pressure of 35 kgf/cm^2, whereas in rabbits exposed to an SF_6-O_2 mixture equivalent in density, it even rose somewhat, as compared to the base level [18]. In another study, where rabbits were exposed to an atmosphere of N_2-O_2 at a pressure of 6 kgf/cm^2, no changes were demonstrated in brain pO_2; however, there was a decrease in oxygenation of arterial blood. But with elevation of pressure to 40 kgf/cm^2, pO_2 of brain tissue dropped [39].

The shortage of information and contradictory nature thereof do not enable us to derive any definite conclusion at this time concerning the effect of the hyperbaric factor on transport of respiratory gases in the body. At any rate, there are no serious grounds to believe that impairment of this transport due to increase in density of the respiratory environment could be the cause of the narcotic effect of neutral gases [45].

Also debatable is the question of whether or not there is a change in intracellular gas exchange in a high pressure atmosphere. There have been reports of decreased O_2 uptake and CO_2 output in some organs of rats exposed to compression of up to 5 kgf/cm^2 [81]. However, other authors do not consider this as any proof of the direct effect of density of the respiratory environment on tissular metabolism [16].

There are several practical considerations that ensue from the facts we have discussed.

It is known that the depths at which a diver or aquanaut can work without being exposed to the adverse effect of hyperbaric conditions can be increased substantially by replacing N_2 in breathing mixtures with He (the density of which is one-seventh that of N_2). While such a replacement at normal atmospheric pressure elicits a beneficial effect on healthy man only in the case of forced breathing [34, 82, 83], at high ambient pressure there is a progressive increase in gain from lowering resistance to respiration by using He-O_2 mixtures [35]. This is confirmed by the data listed in Table 2. At simulated depths of up to 610 m in an atmosphere of He-O_2, alveolar ventilation of the subjects remained normal, both at rest and during minimal exercise [6], whereas in an environment of N_2-O_2 at the same depths (if the narcotic effect could be curbed) man is incapable of physical exertion. Moreover, laboratory mice remained active in an He-O_2 mixture at a pressure of 122 kgf/cm^2, i.e., at a "depth" of more than 1200 m [84].

H_2 could yield an even greater advantage: this gas is half the weight of He (see Tables 1 and 2). According to some data, which are sparse, the H_2-O_2 mixture has a beneficial effect, not only on mechanics of respiration but intrapulmonary exchange of gases [8, 37, 85].

In general, however, as we have seen, no unequivocal results have been obtained as yet concerning the effect of a hyperbaric environment on transport of respiratory gases. The question arises as to whether pO_2 of respiratory mixtures should be raised with increase in depth of submersion. For the time being, there are no grounds for precise recommendations on this score. Prolonged exposure to an atmosphere with pO_2 in excess of 0.3-0.4 kgf/cm^2 may cause oxygen poisoning, and this effect is enhanced under hyperbaric conditions [86, 87]. Observations and theoretical estimates suggest that only a slight increase in oxygen content of inhaled mixtures has a beneficial effect, in accordance with the force of the muscular work performed [40, 88-90].

Within the framework of the problems we have discussed, it is deemed important to conduct an in-depth study of the following: range of ambient pressures and time of exposure to such pressures, within which the respiratory system of a working man can cope with the increased load; patterns of effects of hyperbaric conditions on transport of respiratory gases at all stages, including tissues; correlation between changes in respiration and exchange of gases, on the one hand, and other effects of hyperbaric conditions, for example, their effect on nervous system functions, on the other hand; possibility of optimizing the composition of respiratory mixtures intended for use at specific depths with different physical loads (in particular, a physiological evaluation of an H_2-O_2 environment must be made).

Of course, these questions must be answered with due consideration of all factors that affect man when making deep dives.

BIBLIOGRAPHY

1. Miles, S. "Underwater Medicine," Moscow, 1971.

2. Anishchenko, V. S., and Shulagin, Yu. A. in "Mezhdunarodnyy simpozium po morskoy meditsine. 7-y. Tezisy dokladov" [Summaries of Papers Delivered at 7th International Symposium on Marine Medicine], Moscow, 1976, p 201.

3. Boush, R. L.; Ivanov, A. M.; Sirota, M. G.; et al. Ibid, p 204.

4. Zal'tsman, G. L.; Selivra, A. I.; Arsen'yeva, V. I.; et al. in "Organizm v usloviyakh dlitel'noy giperbarii" [The Organism When Exposed to Hyperbaric Conditions for a Long Time], Leningrad, 1977, pp 57-66.

5. Zal'tsman, G. L. "Physiological Bases for Man's Exposure to High Pressure Ambient Gases," Leningrad, 1961.

6. Bennett, P. B. in "Journees Internationales d'Hyperbarie et de Physiologie Subaquatique," 3d, Paris, 1972, pp 34-43.

7. Broussole, B.; Chouteau, J.; Hyacinthe, R.; et al. in "Underwater Physiology-V," Bethesda, 1976, pp 79-89.

8. Dougherty, J. H. AVIAT. SPACE ENVIRONM. MED., Vol 47, 1976, pp 618-626.

9. Dragonat, P., and Drenckmann, D. EUROP. J. APPL. PHYSIOL. OCCUP. PHYSIOL., Vol 32, 1974, pp 341-348.

10. Fagraeus, L. ACTA PHYSIOL. SCAND., Suppl 414, 1974, pp 1-40.

11. Fagraeus, L., and Bennett, P. B. in "Symposium on Underwater Physiology," 6th, San Diego, 1975, p 33.

12. Guenard, H.; Vieillefond, H.; Timbal, J.; et al. J. PHYSIOL. (Paris), Vol 65, 1973, p 240A.

13. Miles, S., and Mackay, D. E. "Underwater Medicine," London, 1976.

14. Varene, P.; Viellefond, H.; Lemaire, C.; et al. AEROSPACE MED., Vol 45, 1974, pp 161-166.

15. Nikolayev, V. P. IZV. AN SSSR, SER. BIOL. [News of the USSR Academy of Sciences, Biology Series], No 5, 1969, pp 730-735.

16. Selivra, A. I.; Arsen'yeva, V. I.; and Shifrina, K. M. in "Oksibioticheskiye i anoksibioticheskiye protsessy pri experimental'noy i klinicheskoy patologii" [Oxybiotic and Anoxybiotic Processes in the Presence of Experimental and Clinical Pathology], Kiev, 1975, pp 192-193.

17. Troshikhin, G. V. in "Povolzhskaya konf. fiziologov, 6-ya, Materialy" [Proceedings of 6th Povolzh'ye Conference of Physiologists], Cheboksary, Vol 1, 1973, pp 115-116.

18. Shifrina, K. M., and Selivra, A. I. in "Organizm v usloviyakh dlitel'noy giperbarii," Leningrad, 1977, pp 116-122.

19. Yakhontov, B. O. in "Mezhdunarodnyy simpozium po morskoy meditsine, 7-y, Tezisy dokladov," Moscow, 1976, p 226.

20. Broussole, B.; Belnet-Bensimon, E.; Chouteau, J.; et al. J. PHYSIOL. (Paris), Vol 63, 1971, p 118A.

21. Glauser, S. C.; Glauser, E. M.; and Rusy, B. F. ARCH. ENVIRONM. HLTH., Vol 19, 1969, pp 654-660.

22. Kawashiro, T.; Sikand, R. S.; Adaro, F.; et al. RESP. PHYSIOL., Vol 28, 1976, pp 261-275.

23. Kvale, P. A.; Davis, J.; and Schroter, R. C. Ibid, Vol 24, 1975, pp 385-398.

24. Lord, G. P.; Bond, G. F.; and Schaeffer, K. E. J. APPL. PHYSIOL., Vol 21, 1966, pp 1833-1838.

25. Mazzone, R. W.; Modell, H. E.; and Farhi, L. E. RESP. PHYSIOL., Vol 28, 1976, pp 217-225.

26. Miller, J. N. PROC. INT. UNION PHYSIOL. SCI., Vol 12, 1977, p 364.

27. Nielsen, T. M., and Pedersen, O. F. ACTA PHYSIOL. SCAND., Vol 98, 1976, pp 123-130.

28. Uhl, R. R.; Van Dyke, C.; Cook, R. B.; et al. AEROSPACE MED., Vol 43, 1972, pp 836-841.

29. Worth, H.; Takahashi, H.; Willmer, H.; et al. RESP. PHYSIOL., Vol 28, 1976, pp 1-15.

30. Bolotova, N. A. in "Voprosy kliniki, diagnostiki i lecheniya zabolevaniy legkikh" [Problems of Symptomatology, Diagnostics and Treatment of Lung Diseases], Alma-Ata, 1972, p 47.

31. Breslav, I. S.; Zhironkin, A. G.; Isayev, G. G.; et al. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, 1975, pp 136-138.

32. Breslav, I. S., and Khvalibova, R. I. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 2, 1975, pp 19-22.

33. Pogodin, M. A. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 7, 1976, pp 1013-1018.

34. Isayev, G. G.; Pogodin, M. A.; and Khvalibova, R. I. in "Chelovek i zhivotnyye v giperbaricheskikh usloviyakh" [Man and Animals Under Hyperbaric Conditions], Leningrad, 1977, pp 21-27.

35. Beil, M. PNEUMOLOGIE, Suppl 5, 1976, pp 41-60.

36. Palacek, F. in "International Review of Physiology. Respiratory Physiology," Baltimore, 1977, pp 255-290.

37. Fife, W. P. PROC. INTER. UNION PHYSIOL. SCI., Vol 13, 1977, p 225.

38. Behnke, A. R., and Jarbrough, O. D. AM. J. PHYSIOL., Vol 126, 1939, pp 409-415.

39. Troshikhin, G. V.; Batygina, V. N.; and Donina, Zh. A. in "Mezhdunarodnyy simpozium po morskoy meditsine, 7-y, Tezisy dokladov," Moscow, 1976, p 233.

40. Linnarsson, D., and Fagraeus, L. in "Underwater Physiology-V," Bethesda, 1976, pp 55-60.

41. Marchall, L. D.; Lanphier, E. H.; and Dubois, A. B. J. APPL. PHYSIOL., Vol 9, 1956, pp 5-10.

42. Hesser, C. M.; Fagraeus, L.; and Linnarsson, D. in "Symposium on Underwater Physiology," 6th, San Diego, 1975, p 71.

43. Peterson, R. E., and Wright, W. B. in "Underwater Physiology-V," Bethesda, 1976, pp 67-77.

44. Wood, L. D. H.; Bryan, A. C.; Bau, S. K.; et al. J. APPL. PHYSIOL., Vol 41, 1976, pp 206-210.

45. Vail, E. G. AEROSPACE MED., Vol 42, 1971, pp 536-546.

46. Kolchinskaya, A. Z.; Gulyar, S. A.; and Korolev, Yu. N. in "Podvodnyye mediko-fiziologicheskiye issledovaniya" [Medical and Physiological Underwater Research], Kiev, 1975, pp 100-117.

47. Lambertsen, C. J. in "Underwater Physiology-V," Bethesda, 1976, pp 35-48.

48. Kulik, A. M., and Kondrat'yeva, L. N. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1972, pp 29-35.

49. Breslav, I. S. "Voluntary Control of Breathing by Man," Leningrad, 1975.

50. Zinov'yeva, I. D. in "Oksibioticheskiye i anoksibioticheskiye protsessy pri eksperimental'noy i klinicheskoy patologii," Kiev, 1975, pp 92-93.

51. Troshikhin, G. V., and Isaakyan, L. A. Ibid, pp 211-212.

52. Lally, D. A.; Zechman, F. W.; and Tracy, R. A. RESP. PHYSIOL., Vol 20, 1974, pp 117-129.

53. Vorosmarti, J.; Bradley, M. E.; and Antonisen, N. R. UNDERSEA BIOMED. RES., Vol 2, 1975, pp 1-10.

54. Hamilton, R. W. in "Symposium on Underwater Physiology," 3d, Washington, 1967, pp 361-374.

55. Overfield, E. M.; Saltzman, H. A.; Kylstra, J. A.; et al. J. APPL. PHYSIOL., Vol 27, 1969, pp 471-475.

56. Dwyer, H. J., and Pilmanis, A. A. in "Symposium on Underwater Physiology," 6th, San Diego, 1975, p 33.

57. Kurenkov, G. I. in "Mezhdunarodnyy simpozium po morskoy meditsine, 7-y. Tezisy dokladov," Moscow, 1976, p 200.

58. Morrison, J. B.; Butt, W. S.; Florio, J. T.; et al. UNDERSEA BIOMED. RES., Vol 3, 1976, pp 217-234.

59. Salzano, J.; Rausch, D. C.; and Saltzman, H. A. J. APPL. PHYSIOL., Vol 28, 1970, pp 34-41.

60. Schaefer, K. E.; Dougherty, J. H.; and Frayre, R. L. in "Symposium on Underwater Physiology," 6th, San Diego, 1976, p 84.

61. Winsborough, M. M.; Vorosmarti, J.; and McKenzie, J. Ibid, p 32.

62. Chouteau, J.; Cousteau, J.-I.; and Alinat, J. J. PHYSIOL. (Paris), Vol 59, 1967, pp 376-382.

63. Cook, J. C. AEROSPACE MED., Vol 41, 1970, pp 1133-1155.

64. Jarret, A. S. J. APPL. PHYSIOL., Vol 21, 1966, pp 158-162.

65. Lanphier, E. H. BIOMETEOROLOGY, Vol 2, 1967, pp 314-316.

66. Schaefer, K. E. Ibid, pp 327-338.

67. Golovkin, L. G.; Polyakov, V. N.; Tikhonov, M. A.; et al. FIZIOLOGIYA CHELOVEKA [Human Physiology], No 2, 1977, pp 329-335.

68. Wood, L. D. H., and Bryan, A. C. J. APPL. PHYSIOL., Vol 27, 1969, pp 4-8.

69. Nikolayev, V. P., and Shabel'nikov, V. G. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 31, 1975, pp 191-216.

70. Liese, W.; Muysers, K.; and Pichotka, J. P. PFLUG. ARCH. GES. PHYSIOL., Vol 321, 1970, pp 316-335.

71. Sidorenko, L. A., and Shik, L. L. in "Problemy kosmicheskoy biologii," Moscow, Vol 31, 1975, pp 177-190.

72. Martin, R. R.; Zutter, M.; and Anthonisen, N. R. J. APPL. PHYSIOL., Vol 33, 1972, pp 86-92.

73. Georg, J.; Lassen, N. A.; Mellemgaard, K.; et al. CLIN. SCI., Vol 29, 1965, pp 525-532.

74. Lacquet, L. M.; van der Linden, L. P.; and Paiva, M. RESP. PHYSIOL., Vol 25, 1975, pp 157-173.

75. Von Nieding, G.; Krekeler, H.; Muysers, K.; et al. in "Underwater Physiology-V," Bethesda, 1976, pp 61-65.

76. Chouteau, J. in "The Physiology and Medicine of Diving and Compressed Air Work," London, 1969, pp 491-504.

77. Guillerm, R.; Chouteau, J.; Hee, J.; et al. J. PHYSIOL. (Paris), Vol 61, Suppl 2, 1969, pp 307-308.

78. Gulyar, S. A.; Shaparenko, B. A.; Kiklevich, Yu. N.; et al. "Organizm cheloveka i podvodnaya sreda" [The Human Body and the Underwater Environment], Kiev, 1977.

79. Kolchinskaya, A. Z. in "Podvodnyye mediko-fiziologicheskie issledovaniya," Kiev, 1975, pp 8-22.

80. Bennett, P. B. J. APPL. PHYSIOL., Vol 20, 1965, pp 1248-1252.

81. Fati, S.; Pennarola, R.; Santagata, P.; et al. FOLIA MED. (Napoli), Vol 49, 1966, pp 752-768.

82. Bryantseva, L. A.: Dianov, A. G.; Ivanova, R. M.; et al. in "Giperkapniya, giperoksiya, gipoksiya" [Hypercapnia, Hyperoxia and Hypoxia], Kuybyshev, 1974, pp 179-180.

83. Dianov, A. G.; Bryantseva, L. A.: Isayenko, V. V.; et al. in "Dykhatel'naya nedostatochnost' v klinike i eksperimente" [Clinical and Experimental Respiratory Insufficiency], Kuybyshev, 1977, pp 164-165.

84. Macinnis, J.; Dickson, J. G.; and Lambertsen, C. J. J. APPL. PHYSIOL., Vol 22, 1967, pp 694-698.

85. Balouet, G.; Barthelemy, L.; Chouteau, J.; et al. FORSVARSMEDICIN, Vol 9, 1973, pp 301-309.

86. Zhironkin, A. G. "Oxygen—Physiological and Toxic Effects," Leningrad, 1972.

87. Troshikhin, G. V., and Kalacheva, Ye. L. in "Chelovek i Zhivotnyye v giperbaricheskikh usloviyakh," Leningrad, 1977, pp 59-63.

88. Anisimov, Ye. A. in "Vsesoyuznaya nauch. konf. po fiziologii, morfologii, biomekhanike i biokhimii myshechnoy deyatel'nosti, 10-ya. Materialy" [Proceedings of 10th All-Union Scientific Conference on Physiology, Morphology, Biomechanics and Biochemistry of Muscular Function], Moscow, Vol 1, 1968, p 16.

89. Breslav, I. S., and Salazkin, V. N. KOSMICHESKAYA BIOL., No 3, 1977, pp 53-58.

90. Burd, R. J., and Horvath, S. M. INT. Z. ANGEW. PHYSIOL., Vol 28, 1970, pp 263-268.

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CIRCULATION AT REST IN CREW MEMBERS OF THE FIRST MAIN EXPEDITION ABOARD SALYUT-6

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 11-14

[Article by V. A. Degtyarev, V. G. Doroshev, V. M. Mikhaylov, V. S. Georgiyevskiy, S. A. Kobzev, Z. A. Kirillova, N. A. Lapshina, V. G. Savel'yeva and L. V. Umnova, submitted 13 Feb 79]

[English abstract from source]

The cardiovascular studies did not show any abnormalities in systemic hemodynamics of both crewmembers during their 96-day space flight. At an early stage they exhibited distinct variations of certain cardiovascular parameters which later returned to the normal. These changes are characteristic of individual processes of human adaptation to weightlessness.

[Text] We submit here the results of in-depth medical examinations of crew members who participated in the first main expedition involving a 96-day space flight aboard the Salyut-6 orbital station.

Methods

The crew members were usually examined after their days off. We recorded the tachooscillogram of the brachial artery, sphygmogram of the femoral artery, kinetocardiogram of the left (region of the apex beat) and right (4th intercostal space on the right, near the sternum) heart and pressure in an arm cuff using Polinom-2M equipment, with the subjects at rest. For complex evaluation of circulatory function, we determined the heart rate (HR), minimum, mean dynamic, lateral systolic, end systolic and pulse arterial pressure (AP), duration of phases of isovolumetric contraction (IV) and expulsion of blood (EB) by the ventricles. We calculated the rate of propagation of the pulse wave (RPPW) in the aorta, stroke (SV) and minute (MV) volumes of circulation, specific actual (AR) and functional (FR) vascular resistance.

Hemodynamic parameters of crew at rest aboard the Salyut-6 orbital station

Parameter	Before flight	Flight days										
		[illegible]	11	24	30	[illegible]	49	60	70	[illegible]	[illegible]	[illegible]
		Commander										
HR/min	65 (58—78)	63	67	58	62	68	64	65	72	72	64	67
Minimal AP, mm Hg	71 (66—80)	78	75	68	60	63	67	67	65	61	67	60
Mean dynamic AP, mm Hg	99 (87—120)	113	108	100	84	89	91	108	100	100	105	106
Lateral systolic AP, mm Hg	119 (104—142)	132	130	115	98	108	106	120	110	110	113	117
End systolic AP, mm Hg	142 (120—173)	153	159	153	128	140	137	153	147	146	149	150
Pulse AP, mm Hg	48 (32—70)	54	55	47	38	45	40	53	45	49	46	58
RPPW, m/s	5,8 (4,9—7,0)	9,9	9,1	4,9	8,1	6,0	6,8	7,7	7,0	6,1	5,8	5,6
SV, mℓ	124 (86—171)	69	95	145	69	111	92	107	81	111	113	147
MV, ℓ/min	8,2 (5,7—11,3)	4,3	6.3	8,5	4,3	7,6	5,9	7,0	5,9	8,0	7,3	9,8
SR, arbitrary units	21 (15—28)	46	30	21	34	20	27	27	30	22	25	19
Ratio of SR to proper value, %	117	135	127	117	100	99	108	127	120	118	123	125
		Flight engineer										
HR/min	59 (45—65)	60	56	56	59	64	67	67	66	67	64	69
Minimal AP, mm Hg	64 (53—72)	65	54	58	58	62	58	72	66	63	60	58
Mean dynamic AP, mm Hg	87 (73—98)	85	84	78	82	83	78	90	88	82	82	86
Lateral systolic AP, mm Hg	107 (88—120)	109	109	98	99	99	95	105	104	97	97	100
End systolic AP, mm Hg	129 (120—148)	141	140	128	132	138	131	137	142	129	130	148
Pulse AP, mm Hg	41 (39—56)	44	55	40	41	37	37	33	42	34	37	42
RPPW, m/s	6,1 (4,7—7,7)	8,7	8,5	5,8	6,7	6,8	7,0	6,9	5,8	9,7	5,9	6,7
SV, mℓ	177 (77—169)	75	103	119	103	91	95	74	110	50	95	93
MV, ℓ/min	6,9 (4,8—9,1)	4.5	5,8	6,6	6,1	5,8	6,4	4,9	7,3	3,3	6,0	6,6
SR, arbitrary units	25 (19—37)	37	28	23	27	28	24	35	26	48	26	26
Ratio of SR to proper value, %	100	100	100	92	96	96	92	106	109	98	96	100

Note: Range of fluctuations is given in parentheses.

Results and Discussion

There was periodic elevation of AP, associated with increase in SR, during the preflight period in the commander. Pressure was more stable in the flight engineer. Peripheral vascular resistance was consistent with current blood flow rate.

The general condition of crewmen was satisfactory during the mission. In the spacecraft commander, HR was essentially in the preflight range (see Table). His AP was above the mean preflight level on the 7th and 14th flight days due to increased arteriolar tonus. By the end of the first month, it dropped to below base levels. From the 42d day on, there was a tendency toward a second elevation of AP; from the 60th day it became stabilized at the same level, close to the preflight one. Only minimal AP remained somewhat low. As in the preflight period, the cause of AP elevation was constriction of arterioles, as indicated by the fact that actual peripheral resistance was 18-27% above the proper level. There was significant increase in RPPW on the 7th and 14th flight days, with decrease to the lower preflight range by the 24th day; thereafter it usually held at mean preflight levels. SV and MV fluctuated over a wider range in the commander during the 1st flight month than before the flight. Thereafter, the fluctuations decreased, and both parameters remained somewhat lower than the mean preflight levels. By the end of the mission they increased again.

There was virtually no change in HR of the flight engineer up to the 42d flight day, then it began to increase somewhat after the 40th day (see Table). The AP parameters remained within the preflight range throughout the flight. With regard to individual distinctions, it can be noted that minimal, mean and lateral systolic AP remained at the mean preflight levels for the first 2 weeks of the flight, while end systolic pressure rose to maximum preflight levels. Throughout the entire subsequent period, mean and lateral systolic AP were most often below the mean preflight levels, while minimal and end systolic pressure was at the preflight levels. Actual peripheral resistance did not differ appreciably from the proper value. For the first 2 weeks RPPW increased drastically, and thereafter it held at preflight levels. The only exception was the 77th flight day, when the RPPW increased again. SV and MV were essentially in the preflight range, with the exception of the 7th and 77th flight days, when they were lower.

The phase structure of the left ventricle in weightlessness was close to the initial findings in both cosmonauts. However, for the first 2 months there was a distinct tendency toward increased duration of EB. Thus, while it was 0.016 s longer than the proper time for the commander in the preflight tests, it was 0.041 s longer on the 60th day. For the flight engineer, the difference increased from 0.022 s in the preflight tests to 0.038-0.062 s on the 42d-49th flight days. There was some decrease in IC phase of the left ventricle. The demonstrated changes in phases of the left ventricle leveled off significantly on the 60th-70th days, and the main parameters of cardiodynamics differed little from preflight levels at the final stage of the flight. No appreciable changes were demonstrated in the phase structure of the right ventricle. With regard to individual distinctions, we can mention appearance of negligible deviations in duration of different systolic phases of the right ventricle in the flight engineer on the 7th day. These deviations persisted to the end of the mission, and apparently they were adaptive in nature.

Thus, the results of tests conducted at rest did not, on the whole, demonstrate disturbances of systemic hemodynamics in the course of the 96-day flight. The changes that did occur in some circulatory indices were related to adaptation to weightlessness [1] and development of deconditioning [2], somewhat more marked in the flight engineer. The latter may be related to the fact that he did not perform the recommended amount of physical exercise. Indeed, the changes in intracardiac hemodynamics, which were observed on the 42d-60th flight days, leveled off significantly upon subsequent increase in exercise, which is indicative of their transient nature.

The obtained data characterize the general features of the individual process of adaptation of the human circulatory system to weightlessness, which was manifested by marked fluctuation of some parameters of the cardiovascular system at the first stage of the flight with subsequent relative stabilization at a close to preflight level. In ground-based experiments with simulation of the physiological effects of weightlessness, phasic fluctuations were also demonstrated in some parameters of the circulatory system, which were related to processes of adaptation to new functional conditions [3]. Analysis of the obtained data shows that the adaptation process required about 1-1.5 months of the 96-day flight, after which the parameters of the cardiovascular system became rather resistant to extreme factors. In particular, there was a very typical elevation of AP of the commander at the start of the flight with subsequent normalization. Very similar cardiovascular reactions were observed in the crew of the second expedition aboard the Salyut-4 orbital station, in the course of a 63-day space flight. AP rose during the first month of the flight, then dropped [4].

On the whole, the obtained data are consistent with the results of studies referable to prior long-term space flights aboard the Salyut orbital stations, where no appreciable hemodynamic changes were demonstrated in the crew at rest [5, 6], but there were some signs or other of increased functional strain on the cardiovascular system related to the intensive work of the cosmonauts and development of fatigue. It may be assumed that in-depth examinations on so-called medical days, which usually followed days off, were largely instrumental in minimizing fluctuations of some parameters of the cardiovascular system. A certain amount of preventive measures, with satisfactory work and rest schedule, provided for adequate fitness of the crew and aided in successful completion of the mission as a whole.

BIBLIOGRAPHY

1. Parin, V. V.; Bayevskiy, R. M.; and Gazenko, O. G. KARDIOLOGIYA [Cardiology], No 3, 1965, pp 3-11.

2. Kovalenko, Ye. A. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1977, pp 3-9.

3. Pometov, Yu. D. "Distinctive Features of Changes in Gas Exchange and Cardiac Output in Man In Simulation of Some Space Flight Factors," author abstract of candidatorial dissertation, Moscow, 1972.

4. Degtyarev, V. A.; Doroshev, V. G.; Kalmykova, N. D.; et al. KOSMICHESKAYA BIOL., No 6, 1978, pp 9-14.

5. Vorob'yev, Ye. I.; Gazenko, O. G.; Gurovskiy, N. P.; et al. Ibid, No 5, 1976, pp 3-18.

6. Rudnyy, N. M.; Gazenko, O. G.; Gozulov, S. A.; et al. Ibid, No 5, 1977, pp 33-41.

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STATE OF HUMAN BONE TISSUE PROTEIN FRACTION AFTER SPACE FLIGHTS

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[Article by A. A. Prokhonchukov, V. K. Leont'yev, N. A. Zhizhina, R. A. Tigranyan, A. G. Kolesnik and N. A. Komissarova, submitted 18 Apr 78]

[English abstract from source]

Amino acid composition and bone mineralization were studied qualitatively and quantitatively on autopsy of the three crewmembers after their 28-day space flight aboard the orbital station Salyut-1. Sixteen amino acids were detected in the bone protein fraction: cystine and cysteine, lysine, histidine, arginine, aspartic acid, serine, glycine, glutamic acid, threonine, alanine, proline, valine, phenylalanine, leucine and isoleucine, oxyproline. Postflight no abnormalities in the amino acid composition or the bone organic content were found. The role of protein matrices of calcified tissues in mechanisms of bone resistance and adaptation to space flight effects is discussed.

[Text] The question of calcium metabolism during space flights [1-3] is still unclear in many respects, debatable and requires further intensive investigation.

The functional state of protein matrices is the chief factor of dynamic stability (homeostasis) of bone marrow, its resistance and adaptation to various extreme factors. The protein matrices of bone marrow are "nucleators" [?] of hydroxyapatite crystals, the main crystallite of bone tissue most of which consists of calcium and phosphorus salts. Not only mineralization processes, but remineralization (recrystallization) of bone tissue depend on the functional state of the protein matrices. In the presence of various forms of bone pathology related to loss of calcium salts, recalcification (remineralization) is possible only if the functional properties of the protein matrix are retained. Denaturation of protein structures of the bone matrix and loss of their functional properties make bone recalcification impossible, even if there is adequate saturation of the body with calcium and phosphorus salts, and as a result there may be irreversible changes [4-7]. The fat of lyophilized bone homotransplants is a graphic confirmation of this. They do not "take," and after proliferation by vessels from adjacent tissues they are replaced by de novo recipient osseous tissue by means of oppositional growth, since the protein matrices of bone tissue are denatured after lyophilization, and they lose their functional properties [4, 6]. Thus, the bone protein matrices are among the main elements in the mechanisms of fixation of calcium and phosphorus.

However, the crystals of osseous hydroxyapatite are not simply oriented on protein matrices, and are connected to them by chemical bonds. Most authors believe that such a bond is formed by phosphoamino acid phosphate: phosphoserine, phosphothreonine phosphohydroxylisine [8, 9], bound with the calcium of hydroxyapatite. There is also a probable phosphoamide bond between the protein matrix and mineral phase [10-12], as well as involvement of phospholipis in protein mineral interactions [5, 13-15]. Changes in protein metabolism developed in the bones of rats after 100 days of experimental hypokinesia, according to the incorporation of ^{14}C-glycine and impaired binding of ^{32}P-phosphate by bone proteins [16, 17].

The objectives of this study included investigation of the state of the protein fraction of human bone tissue after a flight (autopsy findings on the crew of the Salyut-1 orbital station).

Methods

We used samples of bone tissue from the calcaneus. Lipids were removed with a mixture of ethanol and ethyl ether (1:1), then soft tissues were removed; residues of soft tissues and marrow were removed with papain [18]; the samples were then dried to a constant weight, homogenized and decalcified in a solution of 2 N hydrochloric acid and 96° ethanol for 24 h (4°C temperature) with shaking.

The obtained native collagen was dried, then hydrolyzed in sealed vials of 6 N hydrochloric acid at 110°C for 24 h. The hydrolysate was evaporated under vacuum, dissolved in distilled water and submitted to paper chromatography by the method of T. S. Paskhina [19] as modified by V. K. Leont'yev [20]. Amino acids were assayed concurrently by two methods: calibration charts and standard solutions applied on each chromatogram. We took 2-6 concurrent readings for each sample of ossein. We calculated total protein content of bone tissue as the ratio (percentage) of dry collagen weight to the weight of dry unadulaterated bone.

Amino acid composition was determined in molar percentages without consideration of proline content. Hydroxyproline was demonstrated by the method of Neuman and Logan [21] as modified by A. L. Zaydes et al. [22]. No quantitative assay of proline and cystine was made.

Bone tissue from the calcaneus taken from the cadavers of three men who had died of acute trauma at the age of 20-40 years (without pathoanatomically demonstrable signs of visceral or systemic disease) served as a control for comparative analysis.

We calculated the number of required parallel samples and analyses [23, 24] in order to obtain data with a prespecified confidence level (at least 95%). The data were submitted to statistical processing with the use of Student's criterion [23].

Results and Discussion

Organic fraction and total protein content of bone tissue in the group studied did not differ (P>0.05) from control parameters (Tables 1 and 2), and conformed with data in the literature [4, 25, 26].

Table 1. Organic fraction and total protein content of bone tissue (% dry bone weight)

Constituent	Group	
	under study	control
Organic fraction	36.8±0.9	35.3±0.6
Total protein	28.4±0.7	26.9±0.4

Note: P>0.05 for both parameters.

Analysis of amino acid composition of protein in bone tissue referable to the group under study demonstrated 16 amino acids. Cystine and cysteine (demonstrated together) were present in very small amounts, and they were not assayed thereafter. Lysine and proline were found in all samples; histidine was demonstrated in all samples, but in the form of traces (it was not submitted to quantitative analysis). Threonine was present in small amounts in all samples. Aspartic acid and phenylalanine were present in very small, sometimes trace amounts in all samples.Arginine, glutamic acid, alanine and hydroxyproline were demonstrated in significant and large amounts. Serine, valine, leucine and isoleucine (assayed together) were found in moderate amounts in all specimens. Glycine was present in all samples in the largest amounts (as compared to the other amino acids). A comparison of amino acid composition of bone tissue of the group studied and control group failed to demonstrate qualitative differences. The obtained findings conformed with data in the literature [4, 25, 26].

Quantitative analysis of bone tissue protein in the group under study revealed that it is a type of collagen. Low amounts of cystine, absence of tyrosine, large amounts of aliphatic amino acids, glycine and hydroxyproline were inherent in this protein, as in other collagens. There were relatively minor fluctuations of levels of different amino acids in different samples of the group studied and in parallel readings on the same samples, and they were within the range of the error factor of the reading methods.

Comparative analysis of bones in the group studied and control group failed to demonstrate reliable differences in amino acid composition of total protein (Table 3).

Table 2. Quantitative composition of total bone protein

Amino acid	Main group			Control group		
	1	2	3	1	2	3
Lysine	1,62 (1,31—1,92)	1,97 (1,71—2,22)	1,44 (1,10—1,77)	0,65 (0 –1,30)	2,32 (1,98—2,67)	2,07 (1,67—2,52)
Arginine	8,87 (7,84—10,94)	8,13 (7,72—8,54)	8,50 (8,02—8,98)	6,07 (5,73—6,11)	7,91 (7,07—8,75)	8,24 (7,35 –9,20)
Aspartic acid	1,02 (0,0—2,40)	0 (0)	0,74 (0—1,47)	0 (0)	1,49 (1,31—1,67)	2,18 (1,69—2,67)
Serine	5,11 (4,49—5,89)	4,36 (4,28—4,45)	4,78 (4,27—5,39)	3,43 (2,90—3,96)	5,50 (4,36—6,63)	4,12 (3,41—4,08)
Glycine	33,49 (33,05—34,37)	33,70 (33,40—34,00)	30,20 (29,46—30,93)	33,82 (32,33—35,30)	30,22 (28,30—32,14)	32,82 (32,21—33,14)
Glutamic acid	10,95 (9,25—12,42)	12,08 (11,81—12,35)	11,18 (10,85—11,50)	11,70 (10,91—12,50)	12,04 (12,25—13,04)	12,22 (11,80—12,72)
Threonine	1,40 (0,90—1,60)	1,11 (0,35—1,87)	2,12 (1,77—2,46)	1,19 (1,08—1,30)	1,50 (1,45—1,55)	1,24 (0,61—2,04)
Alanine	18,07 (17,07—18,75)	17,87 (17,53—17,20)	19,85 (15,83—17,87)	19,38 (18,55—20,20)	17,97 (17,33—18,61)	17,51 (15,92—19,50)
Valine	1,96 (0,69—2,77)	1,57 (0,99—2,14)	2,66 (2,12—3,20)	2,62 (1,82—3,41)	1,79 (1,50—2,08)	2,03 (1,63—2,24)
Phenylalanine	0,45 (0,0—1,80)	0,54 (0—1,07)	0 (0)	0 (0)	1,45 (0—2,90)	1,54 (0—4,62)
Leucine + isoleucine	3,49 (2,04—4,98)	3,56 (3,34—3,74)	4,87 (4,29—5,45)	3,53 (2,29—4,77)	2,22 (1,34—3,10)	2,51 (0—5,44)
Hydroxyproline	13,58 (12,99—14,98)	15,40 (14,70—16,09)	16,65 (15,46—17,83)	17,62 (17,50—17,74)	15,17 (13,94—16,40)	14,30 12,94—15,24

Note: Maximum and minimum range of fluctuations is shown in parentheses. The numbers 1 to 3 refer to individual parameters for 3 people in each group.

Table 3. Comparative characteristics of overall amino acid composition of bone protein (in mole %)

Amino acid	Group	
	main	control
Lysine	1,68±0,18	1,66±0,58
Arginine	8,50±0,25	7,41±0,74
Aspartic acid	0,59±0,35	1,22±0,74
Serine	4,75±0,25	4.35±0,70
Glycine	32,46±1,20	32,06±1,24
Glutamic acid	11,40±0,39	12,19±0.32
Threonine	1,54±0.34	1,31±0,18
Alanine	17,60±0,42	18,29±0,64
Valine	2,06±0,37	2,15±0,28
Phenylalanine	0,33±0,18	1,00±0,53
Leucine + isoleucine	3,97±0,47	2,75±0,45
Hydroxyproline	15,21±1,05	15,70±1.13

Note: P>0.05 for all parameters.

The obtained data revealed that no deviations whatsoever that could be interpreted as pathological were demonstrable in the state of bone tissue protein fraction after the space flight. This fact has been established quite clearly on the basis of the results of a complex study of the protein fraction of bone tissue: 1) organic fraction content of bone tissue in the main group did not differ from the control (see Tables 1 and 2); the quantitative and qualitative amino acid composition was identical in the two groups. Data pertaining to amino acid composition of bone tissue protein hold a special place in proof of this thesis. The amino acid composition of total tissular protein is determined by the proportion of individual proteins contained in tissues. The protein of each tissue is characterized by its own unique primary structure and amino acid composition. A change in amino acid composition of total bone protein is a fine indicator of disturbances in tissular protein composition under the influence of various extreme or pathogenic factors. This is particularly important to insoluble tissular proteins, including those of bone, since it is expressly from these indices that one can obtain information about possible changes in these tissues and functional state of protein matrices. This pattern is substantiated by the change in composition of insoluble proteins of decalcified tissues in the presence of various pathological states and diseases.

Thus, on the basis of data in the literature and these studies, it can be concluded that the protein fraction of bone retains its functional properties after a 28-day orbital space flight, including the capacity to fix and retain hydroxyapatite calcium, which was previously demonstrated by direct assay of the mineral fraction, including calcium and phosphorus of skeletal bones [2]. The findings obtained in this study lead us to expound the following hypothesis. Since protein matrices of bone retain their functional properties of fixing calcium and implementing remineralization processes under space flight conditions, it is obvious that various methods and means of stimulating remineralization of bone tissue during space flights are implemented expressly by retention of these properties as determining the main mechanism of remineralization (recrystallization) of bone, which is the basis of its resistance and adaptation to the extreme factors of space flights. This thesis is confirmed by data to the effect that the efficacy of thyrocalcitonin in normalizing bone tissue function is significantly enhanced when it is combined with retabolil [deca-durabolin], which has a selective action expressly on the protein fraction of bone tissue [27].

On the basis of our analysis of the literature and results of the studies, we can expound the assumption (in the nature of a working hypothesis) that the normal state of the bone protein fraction after the space flight could be attributable to the high level of physical training and conditioning of the cosmonauts, with subsequent use aboard the orbital station of the set of equipment and conditioning measures directed toward precluding the undesirable effects of flight factors on man [2, 28, 29].

BIBLIOGRAPHY

1. Kopanev, V. I., and Yuganov, Ye. M. in "Nevesomost'" [Weightlessness], Moscow, 1974, pp 381-428.
2. Gazenko, O. G.; Prokhonchukov, A. A.; Panikarovskiy, V. V.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1977, pp 11-20.
3. Gurovskiy, N. N. MED. GAZETA [Medical Gazette], 5 Aug 1977.
4. G. H. Bourne (editor), "The Biochemistry and Physiology of Bone," New York, Vol 1-3, 1971.
5. Desyatnichenko, K. S. "Proteins of Tooth Enamel Under Physiological Conditions and in the Presence of Pathology," author abstract of candidatorial dissertation, Moscow, 1977.
6. Vaughan, J. M. "The Physiology of Bone," Oxford, 1975.
7. Prokhonchukov, A. A. in "Trudy stomatologov LitSSR" [Works of Stomatologists in Lithuanian SSR], Kaunas, Vol 5, 1970, pp 11-29.
8. Glimcher, M. J., and Krane, S. M. in "Radioisotopes and Bone," P. Lacroix and A. B. Budy, Oxford, 1964, p 393.
9. Veis, A., and Schlueter, R. J. BIOCHEMISTRY, Vol 3, 1964, pp 1650-1657.
10. Solomons, C. C., and Irving, J. T. BIOCHEM. J., Vol 68, 1958, pp 499-503.
11. Leach, S. A. in "International Biochemical Congress," 5th, abstracts of section papers, Sections 1-13, Moscow, Vol 1, 1961, p 95.
12. Wuthier, R. E.; Gron, P.; and Irving, J. T. BIOCHEM. J., Vol 92, 1964, pp 205-216.
13. Irving, J. T. CLIN. ORTHOP., Vol 17, 1960, pp 92-102.
14. Foldes, I.; Vasei, L. I.; and Modis, L. ACTA BIOL. ACAD. SCI. HUNG., Vol 22, 1971, pp 9-18.
15. Haviri, E. LIPIDS, Vol 6, 1971, pp 314-317.
16. Kovalenko, Ye. A.; Popkov, V. L.; Mailyan, E. S.; et al. PAT. FIZIOL. [Pathological Physiology], No 6, 1970, pp 3-9.

17. Prokhonchukov, A. A.; Kovalenko, Ye. A.; Kolesnik, A. G.; et al. STOMATOLOGIYA [Stomatology], No 4, 1970, pp 1-6.

18. Gaydamak, A. N., and Leont'yev, V. K. in "Eksperimental'naya i klinicheskaya stomatologiya" [Experimental and Clinical Stomatology], Moscow, Vol 6, 1975, pp 46-49.

19. Paskhina, T. S. in "Sovremennyye metody v biokhimii" [Modern Methods in Biochemistry], Moscow, Vol 1, 1964, pp 162-180.

20. Leont'yev, V. K. "Proteins of Mineralized Tissues of Healthy Teeth and in the Presence of Caries," candidatorial dissertation, Omsk, 1968.

21. Neuman, R. R., and Logan, M. A. J. BIOL. CHEM., Vol 184, 1950, p 229.

22. Zaydes, A. L.; Mikhaylov, A. N.; and Pushenko, O. I. BIOKHIMIYA [Biochemistry], No 1, 1964, pp 5-7.

23. Urbakh, V. Yu. "Biometric Methods," Moscow, 2d ed., 1964.

24. Hicks, C. "Main Principles Involved in Planning Experiments," Moscow, 1967.

25. Slutskiy, L. I. "Biochemistry of Normal and Pathologically Altered Connective Tissue," Leningrad, 1969.

26. Torbenko, V. I., and Kasavina, B. S. "Functional Biology of Bone Tissue," Moscow, 1977.

27. Bessonova, S. S., and Petrovich, Yu. A. STOMATOLOGIYA, No 1, 1976, pp 8-11.

28. Vasil'yev, P. V. in "Nevesomost'," Moscow, 1974, pp 278-297.

29. Stepantsov, V. I.; Yeremin, A. V.; and Tikhonov, M. A. Ibid, pp 298-313.

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RESEARCH HARDWARE AND HABITAT OF ANIMALS USED IN EXPERIMENT ABOARD COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 18-22

[Article by B. A. Adamovich, Ye. A. Il'in, A. D. Noskin, V. I. Milyavskiy, G. N. Pliskovskaya, V. K. Golov, V. S. Poleshchuk, V. K. Ovcharov and A. A. Shipov, submitted 7 Aug 79]

[English abstract from source]

The paper reviews the hardware used to provide life support to experimental animals (rats) and to obtain information inflight. The hardware includes two specially designed centrifuges to generate artificial gravity. The paper describes the environmental parameters in the mock-up cabin and field laboratories used at the recovery site.

[Text] The next specialized biological satellite, Cosmos-936, was launched in the USSR on 3 August 1977. The research program scheduled for this biosatellite included a continuation of the study of the effects of space flight factors on various biological objects, as well as investigation of the possibility of using artificial gravity [AG] as a means of preventing the adverse effects of weightlessness. The objectives and conditions for the physiological experiments with animals (rats) were described in detail previously [1].

An automated complex of scientific hardware was developed and constructed for the studies aboard Cosmos-936, as was done for the experiments conducted on other biosatellites [2-5]. This complex provided for optimum maintenance conditions for the animals, bioengineering monitoring of their condition, delivering oxygen to animals, removing toxic gas impurities from the pressurized cabin of the biosatellite, maintaining comfortable temperature and humidity levels in the cabin.

The research program for the Cosmos-936 biosatellite differed from others in that mammals were exposed to AG of 1 G, and this was the first time this was done in space. For this purpose, two centrifuges were installed aboard the satellite, each holding five animals (Figure 1). The velocity of rotation of the centrifuges during the flight constituted 53.5±3 r/min, and AG constituted 1 G over a radius of 320 mm (up to the arbitrary longitudinal axis of the animal). Another group of animals was kept in cages that were a part of the automated units analogous to those used in previous flights.

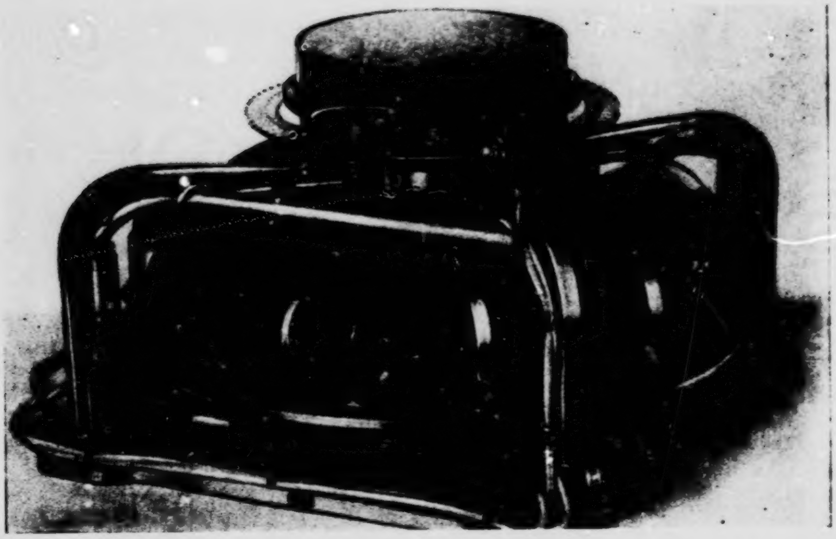

Figure 1. Onboard centrifuge to expose rats to AG

The life support conditions, as well as interior of the cages, both on the centrifuge and in the stationary units were analogous, in spite of their apparent difference externally. There were a feeder, water dish, light fixture, system of ventilation holes, slitted device with a screen to remove excrements and a container for them within the cage. Each cage was equipped with a measuring device that added up the movements made by the rats. Sensors were implanted in some of the animals to measure body temperature.

Essentially the same automated systems for regeneration of the atmosphere were used here as in the experiments on previous biosatellites in order to maintain comfortable temperature and humidity levels in the pressurized cabin, to deliver oxygen to the animals, remove carbon dioxide and toxic gas impurities from the air environment.

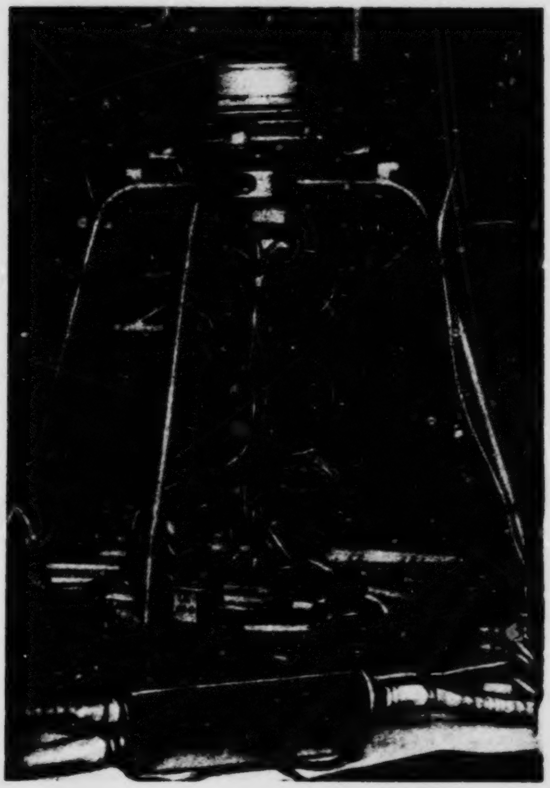

Figure 2. Ground-based short-arm centrifuge for control experiment

During the flight, oxygen content of the descent vehicle constituted 145-210 mm Hg and carbon dioxide did not exceed 14 mm Hg; relative humidity was held at 80-90%.

Much attention was devoted to the quality of the air environment in the cabin, one of the important parameters of which was the amount of toxic gaseous compounds in this environment. The sources of such compounds aboard biosatellites are various polymers, the animals themselves and particularly their liquid and solid excrements. As shown by the results of special studies, there was consistent presence of gas impurities, the main component of which was ammonia, in the air environment of mockups of Cosmos-605, Cosmos-690 and Cosmos-782.

An autonomous system was installed aboard Cosmos-936 to remove gase impurities from the air environment. This system was turned on by command from the ground on the 10th day of the flight, and it was in operation until the mission was completed.

The results of studies of levels of the main gas impurities in the air environment of the mockup of Cosmos-936 revealed that there were trace concentrations of acetone, aldehydes and organic acids. Ammonia and other amino compounds were an exception, and their level reached 8.0 mg/m^3 at the end of the experiment. The concentration of organic compounds was in the range of 48-144 mgO_2/m^3. These findings indicate that the use of a refined system for cleaning the atmosphere aboard Cosmos-936 improved significantly the hygienic conditions of the air environment in the habitat of the experimental animals.

The life support system for the animals, gas analyzers for oxygen, carbon dioxide and water vapor, as well as thermostats and other instruments aboard Cosmos-936 made up a single automated complex. A complex control unit was used to issue and place commands, switch over the electric circuits used for different purposes, communicate with the radiotelemetry and power systems of the satellite.

The ground-based, synchronous control experiment was an important element of the studies aboard Cosmos-936. For this purpose, the same habitat was reproduced in the mockup on the basis of telemetry data delivered from the biosatellite as in the pressurized cabin of the latter during the flight, with the exception of weightlessness and ionizing radiation. The data concerning parameters of the air environment were reproduced in the ground-based experiment with the following error factor: ±2% for oxygen, ±2% for carbon dioxide, ±1% for air temperature and 5-10% for relative humidity. The use of an automatic system of regulating and holding the microclimate parameters aided in such close reproduction of the air environment in the synchronous experiment. This system made it possible not only to maintain rather accurately the microclimate parameters within the required range, but to regulate on an ongoing basis the temperature, humidity and pressure in the sealed space of the mockup of the biosatellite.

Rotation of a group of animals on a short-arm (92 mm) centrifuge (Figure 2) at a rate equal to the rate of the onboard centrifuge was an element of the program for the ground-based control experiments. Two such centrifuges were used, with five animals on each. The purpose of the experiment was to determine the role of the rotation factor in the changes in physiological parameters of animals aboard the biosatellite and exposed to a 1-G artificial gravity.

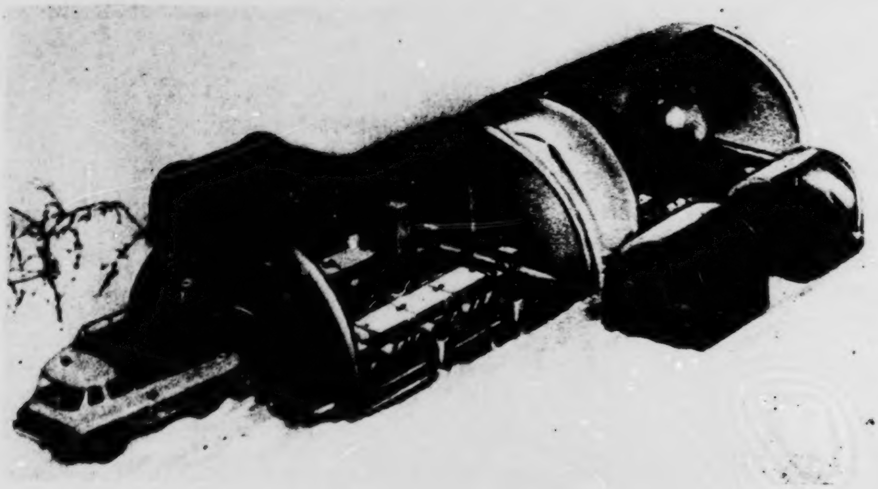

Figure 3. General view of search and rescue complex for conducting scientific research work at the biosatellite landing site

A search and rescue complex, based on a field laboratory, which consisted of a system of inflatable tents with hardware and equipment in them, was developed and constructed for conducting studies at the landing site of the descent vehicle (Figure 3). A total of 50 people could work at the same time in such a laboratory. It was equipped with a miniature power station, air conditioning and microclimate maintaining systems.

The descent vehicle of the biosatellite landed at 0627 hours on 22 August 1977. After 45 min, the descent vehicle was placed in one of the sections of the field laboratory; then the modules were opened, disassembly work was done and the animals were removed. The animals were examined 3.5 h after the descent vehicle landed.

The results of the scientific studies conducted during the experiment aboard Cosmos-936 warrant the belief that the principles serving as the basis for building the life support systems and scientific hardware are valid and have justified themselves entirely.

BIBLIOGRAPHY

1. Il'in, Ye. A.; Korol'kov, V. I.; Kotovskaya, A. R.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1979, pp 18-22.

2. Il'in, Ye. A.; Serova, L. V.; and Noskin, A. D. Ibid, No 3, 1976, pp 9-14.

3. Grigor'yev, Yu. G.; Druzhinin, Yu. P.; Verigo, V. V.; et al. Ibid, No 5, 1977, pp 58-66.

4. Gazenko, O. G.; Genin, A. M.; Il'in, Ye. A.; et al. Ibid, No 6, 1978, pp 43-49.

5. Serova, L. V.; Il'in, Ye. A.; Noskin, A. D.; et al. in "Vliyaniye dinamicheskikh faktorov kosmicheskogo poleta na organizm zhivotnykh" [Effects on Animals of Dynamic Space Flight Factors], Moscow, 1979, pp 7-12.

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PRINCIPAL RESULTS OF PHYSIOLOGICAL EXPERIMENTS WITH MAMMALS ABOARD THE COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 22-25

[Article by O. G. Gazenko, Ye. A. Il'in, A. M. Genin, A. R. Kotovskaya, V. I. Korol'kov, R. A. Tigranyan and V. V. Portugalov, submitted 12 Apr 79]

[English abstract from source]

The program of the 18.5-day flight of the biosatellite Cosmos-936 included studies of physiological effects of prolonged weightlessness (20 rats) and artificial gravity (10 rats). The latter produced a normalizing effect on the function of the myocardium, musculo-skeletal system and excretory system. Simultaneously, artificial gravity exerted an adverse effect on the functions dependent on several sensors, primarily optic, vestibular and motor sensors. It is postulated that the adverse effects are associated with a relatively high rate of rotation and a short arm of the centrifuge.

[Text] The solution of the problem of creating artificial gravity [AG] amounts ultimately to experimental substantiation of the minimal level of gravity at which the adverse effects of weightlessness were eliminated and customary living conditions were provided for the crew.

The AG parameters for manned flights should be determined through direct tests on man. At the same time, experiments with animals make it possible to provide comprehensive substantiation for the use of AG as a means of preventing the adverse effects of weightlessness and, moreover, to assess the negative effects of rotation factors associated with generation of AG.

For the first time in cosmonautic practice, experiments aboard Cosmos-782 biosatellite with plants and lower vertebrates established that the biological effect of AG is basically the same in nature as the effect of earth's gravity. The experiment aboard Cosmos-936, the main objectives and conditions of which were described previously [1], was a logical continuation of the studies pursued aboard the Cosmos-782 biosatellite (1975).

During the orbital flight aboard Cosmos-936, the condition of the animals, as determined according to their overall motor activity and body temperature, was quite satisfactory. The level of overall motor activity was substantially higher, while mean daily body temperature was lower in animals exposed to weightlessness than animals exposed to AG of 1 G (V. S. Oganov, V. Ya. Klimovitskiy).

The long-term flight aboard the biosatellite affected the general condition and postural-motor reactions of the animals in the postflight period. The greatest changes were found in rats exposed to weightlessness. They were sluggish, spent most of the time stretched out; they moved by crawling, or else with drastically altered gait. There were none of the typical movements and positions related to the orienting reaction in a new situation. Less marked changes were noted in animals exposed to AG. They were more active, overcame obstacles well, got up on their hind legs, and their gait was close to normal.

Static endurance, which was diminished after the flight in all cases, was restored sooner in rats exposed to AG, and it also reached the proper level sooner by the 6th day of the postflight period.

There were no appreciable differences in weight gain by experimental groups of animals. However, the rate of weight gain was higher in animals exposed to AG than those in the weightlessness group.

Moderate signs of a stress reaction were noted in animals submitted to weightlessness: increased functional activity of the adrenal cortex, hypoplasia of the thymus and spleen, increased percentage of segmented nuclear neutrophils in peripheral blood, lymphopenia and eosinopenia. Such changes were either absent or extremely insignificant (peripheral blood) in animals exposed to AG.

Microbiological and immunological studies revealed proteus in the throat and decline of class G immunoglobin level in blood serum of animals submitted to weightlessness, unlike those exposed to AG; this was indicative of some weakening of protective properties of their organism.

On the 3d day of the readaptation period, there was a statistically significant decrease in exchange of gases in animals submitted to weightlessness, unlike those exposed to AG during the flight.

The test with a water load (5 mℓ/100 g weight), conducted on the 1st day of the readaptation period to assess the osmoregulatory system and possible liquid shortage in the body, failed to demonstrate any differences in dynamics and maximum levels of diuresis between the two experimental groups of rats. At the same time, there was reliable greater excretion of sodium in urine after the water load test in animals exposed to weightlessness than in rats exposed to AG and in the ground-based control experiments.

Administration of a potassium load (1.25% KCl) on the 2d day of the readaptation period led to virtually the same excretion of fluid in animals from different experimental groups. However, there was greater excretion of potassium (349±24.6 meq/100 g) in animals exposed to weightlessness than in rats submitted to AG (262±43.9 meq/100 g) and animals in the ground-based synchronous experiment (228±2.7 meq/100 g). Thus, the greatest changes in ion regulating function of the kidneys were demonstrated in rats submitted to weightlessness during the flight. AG had a normalizing effect on renal excretion of sodium and potassium.

The absence of any disturbances referable to the structure of individual nephrons of rats in all experimental groups warrants the belief that the changes in electrolyte metabolism (at least the increased excretion of potassium by animals exposed to weightlessness) is the result of a change in basal metabolism and, first of all, metabolism of the muscular system (Yu. V. Natochin).

Exposure to weightlessness led to appearance of distinct signs of atrophy and metabolic disturbances (change in spectrum of lactate dehydrogenase isozymes, accumulation of glycogen, increased phospholipid content and ALT activity) in the muscles of the limbs, particularly the soleus. We observed development of moderate atrophic changes in the same muscles of rats exposed to AG during the flight; however, they usually failed to present metabolic changes.

Both experimental groups of animals presented significant worsening of blood supply to muscles, as indicated by the decreased number of functional capillaries.

Weightlessness led to an increase in amount of sarcoplasmic proteins and significant decrease in ATPase activity of myocardial myosin. No changes were observed in amount of myocardial sarcoplasmic proteins in animals exposed to AG, while the decrease in myosin ATPase was less marked.

Examination of the femoral and tibial bones of rats submitted to weightlessness revealed slower growth rate, development of osteoporosis, decreased density and mineralization, as well as 30% decrease in mechanical bending strength. Use of AG prevented changes in calcium and phosphorus content of long bones.

Studies of the function of the vestibular analyzer revealed that prolonged weightlessness did not alter the function of the semicircular canals (A. A. Shipov), while sensibility of the otolithic system diminished (G. S. Ayzikov). Long-term exposure to a system with AG, on the contrary, failed to alter otolith function; however, it diminished sensibility and reactivity of the semicircular canals. Consequently, in both instances, absence of change in function of one part of the vestibular system is associated with a change in function of the other. This could cause an intralabyrinthine conflict concerning information about a movement. The existence of such a conflict is probably one of the causes of a poor turning reflex and poorer equilibrium function in animals exposed to both weightlessness and AG.

Morphological studies revealed only insignificant ultrastructural changes in the vestibular system, which were equally marked in animals exposed to weightlessness and AG (Ya. Vinnikov).

Examination of higher nervous activity (capacity for orientation in a maze) revealed that the functional changes were more significant in animals kept on the centrifuge during the flight than in those submitted to weightlessness. There was particularly graphic manifestation of this when the tests presented to the rats were more complicated (N. N. Livshits).

Biochemical studies of brain structures responsible for higher motor control revealed that there was the most significant decline in RNA content of Purkinje cells of the cerebellum and decrease in H group content of the tissue of the frontal (motor) cortex of animals exposed to AG during the flight.

Thus, studies of the main physiological systems of rats that were weightless for 18.5 days revealed changes analogous to those demonstrated in previously conducted experiments aboard biosatellites of the Cosmos series [2-4]. These changes can be arbitrarily divided into nonspecific (development of fatigue, decreased nonspecific resistance, appearance of signs of a stress reaction) and specific (change in vestibular function, muscular atrophy, osteoporosis of long bones, changes in the myocardium and excretory system). In most cases, the nonspecific and specific reactions to weightlessness were usually no longer demonstrable by the 25th day of the readaptation period.

Creation of AG of 1 G during the space flight prevented to a significant extent development of the above-mentioned adverse changes in the animals. Special mention should be made of the normalizing effect of AG on the functional state of the myocardium, skeletomuscular system and excretory system. Along with the beneficial effect of AG on the animals, we found some adverse effects on functions, the performance of which is implemented by the concurrent activity of several analyzers, first of all the visual, vestibular and motor (function of equilibrium, turning and landing reflex, orientation in the maze and higher motor control).

The demonstrated differences in the tested parameters of animals exposed to AG and natural gravity are probably attributable to the relatively high rate of rotation of the centrifuge (53.3 r/min) and its short arm (320 mm).

BIBLIOGRAPHY

1. Il'in, Ye. A.; Korol'kov, V.I.; Kotovskaya, A. R.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1979, pp 18-22.

2. Il'in, Ye. A.; Serova, L. V.; and Noskin, A. D. Ibid, No 3, 1976, pp 9-14.

3. Grigor'yev, Yu. G.; Druzhinin, Yu. P.; and Verigo, V. V. Ibid, No 5, 1977, pp 58-66.

4. Gazenko, O. G.; Genin, A. M.; Il'in, Ye. A.; et al. Ibid, No 6, 1978, pp 43-49.

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SEMICIRCULAR CANAL FUNCTION IN RATS AFTER FLIGHT ABOARD THE COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 25-30

[Article by A. A. Shipov and V. G. Ovechkin, submitted 26 Dec 78]

[English abstract from source]

The nystagmic reflex, latent period, total and mean number of events, and their duration were measured in the rats flown for 18.5 days aboard the biosatellite Cosmos-936 under the conditions of weightlessness and artificial gravity. The studies demonstrated that prolonged weightlessness did not influence the receptor formations and centers of semi-circular canals. A long exposure to artificial gravity brought about a decrease in reactivity and sensitivity of semi-circular canals. The mechanisms of these phenomena are discussed.

[Text] Substantial disturbances referable to postural and certain motor reactions were demonstrated in rats after an 18.5-day flight aboard the Cosmos-782 biosatellite. Generally, the findings were indicative of temporary functional insufficiency of the motor and vestibular analyzers [1]. For this reason, much attention was devoted to the study of vestibular function in the experiment aboard Cosmos-936. It was of special interest to study the group of animals exposed to artificial gravity [AG]. The fact of the matter is that vital functions of animals in a rotating system are related to prolonged exposure of the body and, in particular, the vestibular system, to Coriolis and precessional accelerations [2]. Such factors can lead to a change in vestibular function, locomotion, opticomotor coordination and, ultimately, to impairment of equilibrium.

In this work we submit the results of a comparative study of the functional system [3] of the semicircular canals of rats after flying aboard Cosmos-936 in weightlessness and under AG of 1 G.

Methods

Experiments were conducted on 25 male SPF Wistar rats with an initial weight of 210-230 g. The animals were divided into 5 equal groups: FW_3

and FC_2--animals flowing in space for 18.5 days and exposed to weightlessness and AG, respectively; SW_3--rats used in a ground-based synchronous experiment, in which the habitat aboard the biosatellite and dynamic factors inherent in the launching, descent from orbit and landing phases were simulated; C_2^0--animals rotated in a short-arm ground-based centrifuge at the rate of 53.3±0.3 r/min, with the same angular velocity of rotation of the onboard centrifuge and, finally, VC_3--animals in the vivarium control. The existence of three ground-based control groups made it possible to differentiate between the influence of the factors of weightlessness, rotation (precessional and Coriolis accelerations), upkeep conditions, as well as repeated tests for changes in the reactions studied. The experimental conditions aboard Cosmos-936 were described in detail previously [4].

We assessed the function of the semicircular canals according to changes in characteristics of the nystagmic reflex in response to a series of increasing angular accelerations (10, 20, 30, $40°/s^2$). The animals were rotated on a trapezoidal program: positive acceleration for 3 s, rotation at a constant rate for 1 min, negative acceleration. With each acceleration they were rotated once, and the direction of rotation for each subsequent acceleration was the opposite of the preceding one [5].

Nystagmus was assessed on the basis of the latency period (measured from the start of rotation to the start of the rapid phase of the first nystagmic jerk), number of jerks, duration and mean frequency of jerks (quotient from dividing the number of jerks by duration of nystagmus).

The animals were examined 2 weeks before the flight and start of ground-based control experiments, as well as on the 2d, 7th, 12th, 15th and 23d days of the readaptation period. The landing day was considered as 0 day of the readaptation period.

The obtained data were submitted to statistical processing, with the use of Student's criterion ($P<0.05$).

Results and Discussion

Background tests revealed that the correlation between the nystagmus parameters studied and magnitude of acceleration did not differ basically from the one previously described [6-10].

In the VC_3 group of animals, successive testing of the latency period of nystagmus did not differ from the background findings. The number of jerks, duration and frequency of nystagmic jerks decreased from test to test. The decline of nystagmus parameters was indicative of habituation to angular accelerations at the subsequent examinations [9-10].

At all tested times and with all levels of accelerations used, we failed to demonstrate reliable differences between the FW_3, SW_3 and VC_3 groups with regard to such parameters as latency period, number of jerks (with the exception of acceleration of 40°/s on the 2d day), duration (Figure 1) and frequency of nystagmic jerks. Thus, long-term weightlessness did not cause an appreciable change in sensibility and reactivity of the functional system of the semicircular canals or nature of habituation to repeated exposure to angular accelerations.

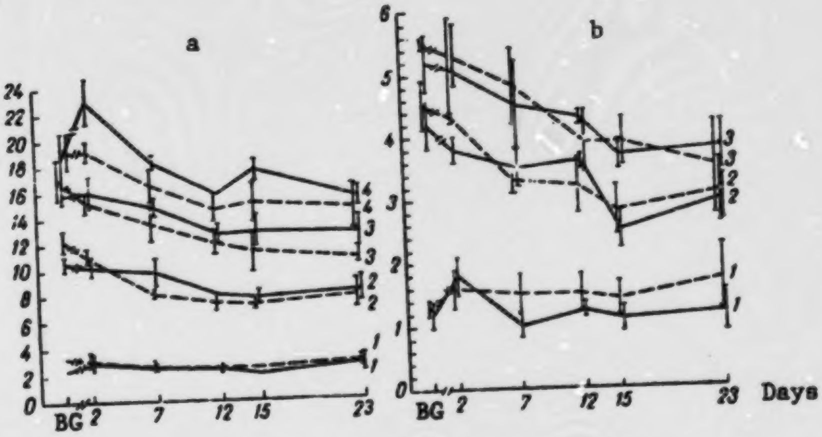

Figure 1. Number of nystagmic jerks (a) and duration of nystagmus (b, in seconds) during rat readaptation following 18.5-day flight aboard Cosmos-936 in weightlessness. The solid line refers to the FW_3 group and the dash line to SW_3. X-axis, day of examination. 0 day refers to day of end of experiment. 1-4—accelerations of 10, 20, 30 and 40°/s^2, respectively. BG—background.

Very different patterns of changes in the parameters tested were found in animals rotated on the centrifuge upon analysis of their nystagmic reaction. On the 2d postflight day, a distinct tendency toward longer latency period of the nystagmic reaction to accelerations of all tested levels was observed in the FC_2 group of animals (Figure 2). The C_2^0 group also presented an increase in latency period, which was reliable with accelerations of 10, 20 and 30°/s^2. On the 7th day, the duration of the latency period of nystagmus did not differ from the background levels with accelerations of 20, 30 and 40°/s^2. With 10°/s^2, restoration of the latency period took a longer time (see Figure 2). We failed to demonstrate reliable differences between animals in groups FC_2 and C_2^0, with regard to latency period of the nystagmic reaction. Thus, when animals were kept in a rotating system for a long time there was temporary increase in latency period of the nystagmic reaction, i.e., decreased sensitivity of functional systems of the semicircular canals to angular accelerations. It should be noted that Clark [11], who studied the latency period of nystagmus in rats following prolonged (up to 60 days) rotation on a ground-based centrifuge (41 cm radius, 62 r/min, 2 G), also observed a reliable increase. Comparable results were also obtained from analysis of the thresholds of the nystagmic reaction of rabbits after 15 days of rotation on a centrifuge (100 cm arm, 3 r/min) [6]. The increase in latency period of the electromyographic reaction of muscles of rat hind legs to rotation of the animals about the longitudinal body axis [12], increase in spontaneous motor activity of rats upon repeated placement in a revolving system [13], as well as data [14] pertaining to a decrease in threshold sensitivity of chickens to angular accelerations after prolonged rotation (180 cm arm, 25 r/min, 1.5 G for 35 days and 30 r/min, 2 G for 49 days) are also indicative of decreased sensitivity to vestibular stimuli after being kept in rotating systems. Our studies supplement the findings of the above authors in that they demonstrate the brief nature of increased thresholds of sensitivity of the semicircular canals according to indices of somatic reactions to angular accelerations. In our opinion, the longer time required for restoration of the latency period of nystagmus with the lowest of the tested accelerations ($10^\circ/s^2$) is attributable to the fact that this parameter is particularly sensitive to the state of the central nervous system [8, 15], which changes appreciably after rotation [16], in the case of using low accelerations.

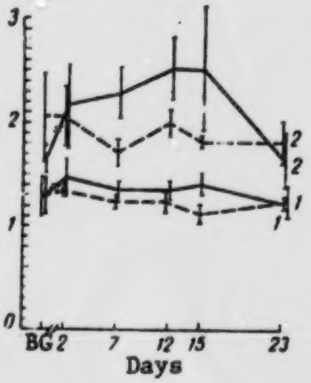

Figure 2.
Latency period of nystagmus (s) in rats after 18.5-day flight aboard Cosmos-936 with AG; Solid line, FC_2 group; dash line FW_3; 1 and 2--20 and $10^\circ/s^2$ accelerations, respectively; BG--background.

Examination on the 2d day of the aftereffect period revealed a reliable decrease in number of nystagmic jerks in animals of groups FC_2 and C_2^0, as compared to both background levels and data for animals in groups FW_3, SW_3 and VC_3. Figure 3a illustrates this on the example of change in nystagmic reaction to $30^\circ/s^2$ acceleration. There was a high level of significance of differences with accelerations of 40, 30 and $20^\circ/s^2$ ($P<0.001$). The routine examination on the 7th day of the readaptation period revealed that the number of nystagmic jerks not only failed to decrease, as compared to the 2d day, it even increased, and the higher the acceleration level, the more it increased. In group C_2^0 animals, this increase was reliable with all tested levels of accelerations, and in group FC_2, it was reliable with accelerations of $20^\circ/s^2$. Thereafter, there was slower increase in number of jerks, and this was followed by a tendency toward decrease (Figure 3a). However, even on the 23d day, the number of nystagmic jerks was greater than on the 2d day. Analogous patterns were inherent in the curves of duration of nystagmus (Figure 3b). The curves of dynamics of frequency of nystagmic jerks show only a tendency toward such changes. The parameters of nystagmus were the same in all groups of animals on the 7th-12th days. At all times tested, we failed to demonstrate differences in reactions to acceleration and deceleration of rotation according to all of the tested parameters of nystagmus.

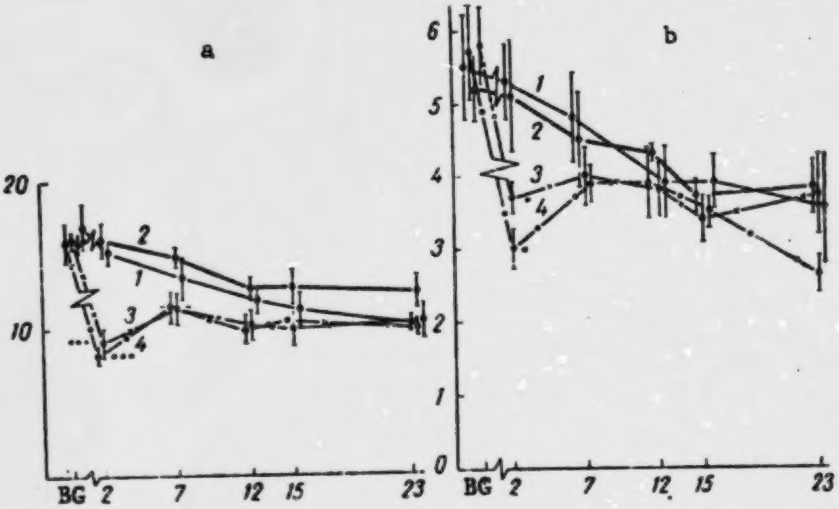

Figure 3. Number of jerks (a) and duration of nystagmus (b; in s) in rats during readaptation period after 18.5-day flight aboard Cosmos-936 with AG. In all cases angular acceleration constituted $30°/s^2$.

BG) background
1-4) SW_3, FW_3, FC_2 and C_2^0 groups, respectively
*) $P<0.05$, as compared to indices for group SW
***) $P<0.001$

A decrease in some parameters of the nystagmic reaction was observed in man during prolonged presence in a rotating system [17, 18]. In experiments conducted on chickens, it was found that there was significant decrease in the nystagmic reaction when first tested on the day of termination of prolonged rotation; it increased thereafter, which is indicative of disappearance of habituation to repeated exposure to angular accelerations [14]. It was also noted that the higher the level of gravity at which prolonged rotation occurred, the more significant the initial decrease in the reaction and the fuller its restoration at subsequent tests. In our study, we observed a similar change in nystagmic reaction of animals in groups FC_2 and C_2^0, but it was less marked (see Figure 3).

In our opinion, the unique dynamics of parameters of the nystagmic reaction, as demonstrated in the successive tests during the aftereffect period following prolonged rotation, are indicative of onset of complex residual [trace] processes in the nystagmogenic centers. These processes are induced by prolonged and combined stimulation of receptors of the semicircular canals by precessional accelerations and receptors of the otolith system by Coriolis accelerations, which arise with spontaneous head movements in the rotating system. Indeed, with concurrent stimulation of both parts of the vestibular system during eccentric rotation, subsequent stimulation only of receptors of the semicircular canals induces changes in parameters of nystagmus [19] similar to those we demonstrated.

Thus, analysis of the changes in nystagmic reaction of rats (according to such parameters as latency period, number of jerks, duration and mean frequency of jerks) in response to a series of accelerations increasing in level failed to demonstrate appreciable changes, i.e., the sensitivity and reactivity of the functional system of the semicircular canals did not change in animals after exposure to weightlessness. This may indicate that prolonged weightlessness does not affect receptor elements and centers of the semicircular canals. Perhaps, these influences are so insignificant and brief that they cannot be demonstrated on the 2d day after landing.

Prolonged stays of animals in a system with AG leads to a decrease in reactivity and temporary decrease in sensitivity of the functional system of the semicircular canals during the aftereffect period, as a result of prolonged and concurrent stimulation of the semicircular canals by precessional accelerations and receptors of the otolith system by Coriolis accelerations. The temporary decrease in sensitivity of the functional system of the semicircular canals could lead to a need for use of considerably higher angular accelerations for an animal placed in a situation that makes it difficult to retain equilibrium (mobile or unstable support, narrow bar) in order to alter muscle tone of antigravity muscles when equilibrium is impaired. Under such conditions, we could expect an increase in amplitude of angular movements of the head and body, and rapid loss of equilibrium due to the impossibility of fine control of postural tonus by the vestibular analyzer [11].

BIBLIOGRAPHY

1. Kotovskaya, A. R.; Shipov, A. A.; Ayzikov, G. S.; et al. in "Vliyaniye dinamicheskikh faktorov kosmicheskogo poleta na organizm zhivotnykh" [Effects of Dynamic Space Flight Factors on Animals], Moscow, 1979, pp 129-135.

2. Sarkisov, I. Yu., and Shipov, A. A. IZV. AN SSSR. SER. BIOL. [News of the USSR Academy of Sciences, Biology Series], No 3, 1974, pp 425-428.

3. Anokhin, P. K. "Biology and Neurophysiology of Conditioned Reflexes," Moscow, 1968.

4. Il'in, Ye. A.; Korol'kov, V. I.; Kotovskaya, A. R.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1979, pp 18-22.

5. Shipov, A. A., and Ovechkin, V. G. Ibid, No 5, 1978, pp 68-72.

6. Grigor'yev, Yu. G.; Farber, Yu. V.; and Volokhova, N. A. "Vestibular Reactions," Moscow, 1970.

7. Fluur, E., and Mendel, L. ACTA OTO-LARYNG. (Stockholm), Vol 61, 1966, pp 463-474.

8. Idem, Ibid, Vol 68, 1969, pp 127-136.

9. Shipov, A. A. KOSMICHESKAYA BIOL., No 4, 1970, pp 66-70.

10. Bokhov, B. B., and Shipov, A. A. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 9, 1965, pp 59-62.

11. Clark, D. L. BEHAV. BIOL., Vol 12, 1974, pp 509-516.

12. Gyurdzhian, A. A., and Apanasenko, Z. I. DOKL. AN SSSR [Reports of the USSR Academy of Sciences], Vol 156, No 1, 1964, pp 225-227.

13. Roccio, C.; Igarashi, M.; and Eckin, A. ANN. OTOL. (St. Louis), Vol 76, 1967, pp 179-188.

14. Winget, C. M.; Smith, A. H.; and Kelly, C. F. J. APPL. PHYSIOL., Vol 17, 1962, pp 709-711.

15. Fluur, E., and Mendel, L. ACTA OTO-LARYNG. (Stockholm), Vol 68, 1969, pp 201-214.

16. Fedorov, V. K.; Obraztsova, G. A.; and Nudman, S. I. DOKL. AN SSSR, Vol 160, No 3, 1965, pp 734-736.

17. Guedry, F. E.; Graybiel, A.; and Collins, W. E. AEROSPACE MED., Vol 33, 1962, pp 1356-1360.

18. Galle, R. R., and Yemel'yanov, M. D. KOSMICHESKAYA BIOL., No 5, 1967, pp 72-79.

19. Gusev, V. M.; Kislyakov, V. A.; Orlov, I. V.; et al. "Mechanisms of Interaction of Vestibular System Receptors," Leningrad, 1978.

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ROLE OF DYNAMIC SPACE FLIGHT FACTORS IN THE PATHOGENESIS OF INVOLUTION OF LYMPHATIC ORGANS (EXPERIMENTAL MORPHOLOGICAL STUDY)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 30-35

[Article by A. S. Kaplanskiy and G. N. Durnova, submitted 5 Sep 78]

[English abstract from source]

The role of the dynamic factors in accidental involution of lymph organs has been investigated in a ground-based study simulating a 20-day space flight. It has been inferred from the study that lymph organ involution observed in rats exposed to prolonged space flights is caused by chronic and acute stresses. Chronic stress is associated with weightlessness and leads to hypoplasia of lymph organs; acute stress is connected with the transition from weightlessness to normal gravity (gravity stress), thus enhancing chronic stress induced lymph tissue hypoplasia. Spleens of both weightless and hypokinetic rats show inhibition of erythropoiesis and accumulation of hemosiderine due to accelerated erythrocyte degradation caused by diminished motor activity.

[Text] In previous studies [1-3], it was often observed that there is accidental involution of lymphatic organs of rats that spent a long time aboard a biosatellite. Development of hypoplasia of lymphatic tissue of animals was interpreted as a result of the stressor effect of the extreme factors of the space flight. However, the significance of each of them to the pathogenesis of lymphatic hypoplasia remained unclear, since the changes demonstrated in lymphatic organs of rats after landing of biosatellites constituted the overall effect of several such factors, which were active at different phases of the space flight.

In this study, we have tried to determine the role of weightlessness and other extreme space flight factors in development of lymphatic hypoplasia, and we used for this purpose the results obtained from a ground-based model experiment.

Methods

Experiments were conducted on 74 male Wistar rats from an SPF colony, with initial weight of about 240 g. We simulated stressor factors, which occur during launching and landing of biosatellites, as well as gravitational stress, which develops when changing from weightlessness to earth's gravity, by means of 5-h immobilization on special stands, with the animals in prone position, using a method developed at the Institute of Experimental Endocrinology of the Slovak Academy of Sciences [4, 5]. To simulate weightlessness in the ground-based experiment, we put the animals in small box-cages, which restricted movement, for 20 days (the time corresponding to mean duration of biosatellite flights). The data of a number of authors, indicating that hypokinesia under ground-based conditions reproduces rather well the main biological effects of weightlessness [6-8] served as grounds for using hypokinesia as a model of weightlessness.

All of the animals were divided into 7 groups: the 1st, 2d and 4th groups consisted of 5, 9 and 5 rats, respectively, which were sacrificed immediately, 5 h and 20 days after 5-h immobilization; the 3d group consisted of 10 animals sacrificed immediately after 10-h immobilization; the 5th consisted of 5 rats submitted to hypokinesia for 20 days after 5-h immobilization; the 6th consisted of 9 rats submitted to 5-h immobilization twice (20-day interval); the 7th consisted of 10 animals that were immobilized for 5 h, kept under hypokinetic conditions for 20 days and then submitted again to 5-h immobilization. We used 25 intact rats as a control; they were kept in the vivarium and sacrificed at the same times as experimental animals. We weighed the thymus and spleen of experimental and control rats, then fixed them in Carnoy fluid and imbedded them in paraffin. Organ sections were stained with hematoxylin-eosin, methyl green-pyronine and picrofuchsin. We measured the area of white pulp of the spleen using enlarged photographic prints of spleen cross sections. [9].

Results and Discussion

According to the data listed in the Table, there was no decrease in weight of the thymus and spleen of rats in the 1st group, whereas animals in the 2d and 3d groups presented a decrease in spleen weight with no change in the thymus. In the 4th group of rats, the weight of the thymus and spleen did not differ from that of control animals. At the same time, there was a decrease in thymus weight of rats in the 5th group, and there was a distinct tendency toward decrease in spleen weight. The second 5-h immobilization 20 days after the first immobilization for the same time (6th group) led to a decrease in spleen weight, with no change in the thymus. Finally, in the case of repeated immobilization of the rats following the first 5-h immobilization and 20 days of hypokinesia (7th group), there was a decrease in weight of the thymus and spleen.

Histological examination of the thymus of rats in the 1st, 2d and 3d groups revealed massive accumulations of nuclear detritus, due to massive breakdown of lymphocytes, in the cortical substance of all animals. In the rats of the 2d and 3d groups, there was the same amount of nuclear detritus, which was considerably greater than in the thymus of the 1st group of rats.

Along with nuclear detritus in the cortical substance of the thymus in rats of the 2d and 3d groups, we encountered numerous macrophages that phagocytized the nuclear detritus (there was no macrophage-phagocytic reaction in the thymic cortex of rats in the 1st group). In all three of the groups mentioned, there was some vagueness of the boundary between the cortical and medullary substance.

Thymus and spleen weight, area of white pulp of spleen in experimental and control rats (M±m)

Group	Nature of experiment	Wt. of thymus mg	P	Wt. of spleen mg	P	White pulp area in arbitrary units	P
1	Immobilization, 5 h (n=5)	606±26	<0,4	555±53	<0,2	502±62	<0,5
	Vivarium control (n=5)	650±39		670±58		483±39	
2	Immobilization, 5 h, + 5-h rest (n=9)	444±39	<0,4	415±14	<0,001	262±13	<0,001
3	Immobilization, 10 h (n=10)	483±27	<0,9	421±9	<0,001	333±41	<0,05
	Vivarium control (n=9)	488±22		558∓14		464∓40	
4	Immobilization, 5 h, + 20 days in vivarium (n=5)	580±52	<1,0	692±79	<0,9	476±86	<0.3
5	Immobilization, 5 h, + 20 days of hypokinesia (n=5)	360±66	<0,02	578±39	<0,1	507±39	<0,2
6	Immobilization, 5 h, + 20 days in vivar. + 5-h immobilization (n = 5)	547±29	<0,5	578±30	<0,05	410±69	<0,05
7	Immobilization, 5 h, + 20-day hypokinesia + 5-h immobilization (n=10)	446±41	<0,02	450±28	<0,001	365±35	<0,001
	Vivarium control (n=11)	583±31		679±23		585±23	

Histologically, the spleen of rats in the 1st group did not differ appreciably from control findings, with the exception of some increase in number of mature neutrophils in the red pulp. According to the data listed in the Table, there was no decrease in area occupied by the white pulp of the spleen. In rats of the 2d and 3d groups, unlike those in the 1st, we observed significant decrease in area of white pulp of the spleen (see Table), but it was not associated with death of lymphocytes and appearance of nuclear detritus in the lymphatic follicles. Intensive neutrophil infiltration was demonstrated in the red pulp of the spleen of rats in the 2d and 3d groups: large and small focal accumulations of mature neutrophils were encountered everywhere in the red pulp.

The histology of the thymus and spleen of rats in the 4th group did not differ from control findings.

In the 5th group of animals, the lobules of the thymus were somewhat reduced in size, the layers of interlobular connective tissue were slightly thickened, while the cortical substance of the lobules was reduced; a moderate amount of macrophages with clear cytoplasm was demonstrated in the cortical substance of the thymus. In the spleen of this group of rats, we demonstrated some decrease in size of lymphatic follicles and decreased cellularity, although no reliable decrease in white pulp area was noted (see Table). In the red pulp of the spleen, there was distinct inhibition of erythroid hemopoiesis, as indicated by the reduction in size and number of focal accumulations of immature erythroid cells. In addition, there was intracellular and extracellular accumulation of hemosiderin in the red pulp.

The histology of the thymus and spleen of rats in the 6th group differed little from that of the 1st group; the difference only consisted of the fact that, in the 6th group, there was a statistically reliable decrease in weight of the spleen and area of white pulp (see Table).

The most marked histological changes in the thymus and spleen were found in the 7th group of rats. Their thymus lobules were somewhat reduced in size, the interlobular connective tissue was slightly thickened and cortical substance of the thymus was constricted. Massive accumulations of nuclear detritus were found in the cortical substance of the thymus, and the amount thereof was greater in this group than in the 6th group.

The spleen of rats in the 7th group presented a distinct decrease in size of lymphoid folicles and area of white pulp (see Table). The decrease in size of lymphoid follicles occurred mainly due to loss of lymphocytes, as a result of which there was better demonstration of reticular stroma. In addition to the decrease in lymphocyte number, we encountered small accumulations of nuclear detritus in the follicles, which were not found in other groups. In this group of rats, there was neutrophil infiltration of the red pulp of the spleen, drastic decrease in number and size of sites of extramedullary erythropoiesis, intracellular and extracellular accumulation of hemosiderin.

The changes observed in rat lymphatic organs can be divided into two main types: the first includes changes such as massive breakdown of cortical lymphocytes of the thymus, hypoplasia of lymphoid tissue of the spleen, neutrophil infiltration of red pulp; the second refers to inhibition of erythroid hemopoiesis in the spleen and accumulation of hemosiderin in it. The first group of changes is a morphological manifestation of stress [10-12], whereas changes of the second type are not related to development of the reaction of the general adaptation syndrome, and they are consistently observed with muscular inactivity [13, 14].

During the hisotlogical examination of the thymus and spleen of rats that were submitted to acute immobilization stress, we were impressed by the differences in nature of reactions of the thymus and spleen to single exposure to the extreme factor. Thus, with acute stress, there was massive breakdown of lymphocytes in the thymus with subsequent development of the macrophage-phagocytic reaction (we cannot rule out the possibility of migration of lymphocytes from the thymus), whereas in the spleen no death of lymphocytes was observed, and the reduction of lymphoid tissue apparently occurred chiefly as a result of migration of lymphocytes [15-17]. There was much faster migration of lymphocytes from the spleen than elimination of destroyed lymphocytes from the thymus, as a result of which the weight of the spleen and area occupied by its white pulp were decreased as early as 10 h after onset of stress (2d and 3d groups); at this time there was still no decrease in weight of the thymus.

A comparison of the changes in the thymus and spleen of rats in the 1st and 2d groups, as well as the 3d group, warrants the statement that the changes in lymphatic organs due to stress reach maximum development 10 h after the start of immobilization of the animals and that 10-h immobilization stress does not worsen the severity of lesions to lymph organs, as compared to 5-h stress.

The absence of any changes in the thymus and spleen of rats in the 4th group, as compared to control findings, indicates that a 20-day period is quite sufficient for restoration of cellular composition and structure of lymphatic organs of rats submitted to acute immobilization stress.

As indicated above, the combination of 5-h immobilization and subsequent hypokinesia leads to hypoplasia of lymph organs. The integrity of typical structure of these organs warrants the belief that there is at least partial restoration of cellular composition of lymphatic organs following acute stress, in spite of hypokinesia. It should be noted that, along with the decrease in amount of lymphoid tissue, the loss of immature erythroid cells, which occurred due to inhibition of erythroid hemopoiesis, could also play a substantial role in reducing the weight of the spleen of rats submitted to hypokinesia.

The second 5-h period of immobilization 20 days after the first (6th group) led to development of changes in the rat thymus and spleen that were similar to those observed after single exposure to immobilization stress. At the same time, in rats submitted to immobilization a second time after 20 days of hypokinesia, the damage to lymphatic organs was appreciably greater than in animals submitted to immobilization a second time after spending 20 days in the vivarium, as manifested by the increase in number of disintegrated lymphocytes in the thymus and appearance of nuclear detritus in the lymphoid follicles of the spleen. Intensification of destructive processes induced by stress in lymph organs of rats following hypokinesia is perhaps attributable to a change in reactivity of the animals during long-term restriction of motor activity, since we know that hypokinesia lowers resistance of the organism to subsequent extreme factors [18]. As shown by previous studies [1-3], there was massive breakdown of cortical lymphocytes of the thymus and moderate disintegration of lymphocytes in follicles of the spleen and parafollicular zone of lymph nodes, neutrophil infiltration of red pulp, hypoplasia of lymphoid tissue of the thymus and spleen, inhibition of erythroid hemopoiesis in the spleen and accumulation of hemosiderin in it in rats after flights aboard biosatellites. In view of the fact that such acute changes as breakdown of lymphocytes in lymph organs and neutrophil infiltration of the spleen reach maximum development about 10 h after the start of exposure to the stressor (results of the model experiment), there is every reason to believe that the development of analogous changes in rats that were exposed to weightlessness is related to acute gravitational stress, which occurred when the animals changed from weightlessness to earth's gravity. This is indicated by the absence of changes inherent in acute stress in lymph organs of rats exposed to artificial gravity of 1 G while aboard Cosmos-936, as well as the absence of lesions to lymph organs of rats submitted to accelerations in the ground-based experiment, which were equivalent to those that animals are subjected to during a biosatellite landing. As for acute changes in rat lymph organs that could be related to the effects on the animals of the extreme factors associated with lift-off and transition to weightlessness, there were barely traces thereof in lymph organs after 20 days of space flight, since there was restoration within this time of structure and cellular composition of lymph organs, as shown by our model experiment.

However, it would be wrong to believe that the involution of lymph organs observed in rats in the postflight examination was the result of gravity stress alone. According to the data obtained from the model experiment, prolonged hypokinesia leads to development of hypoplasia of lymphoid tissue. Consequenlty, restriction of motor activity of the animals during the space flight could also be one of the causes of involution of lymph organs. In order to determine whether weightlessness has a stressor effect on the body, inducing hypoplasia of lymphoid tissue, let us consider the results of weighing the thymus of rats flown about Cosmos-782 and Cosmos-936 artificial satellites of earth. The thymus weighed less in rats that were weightless during the space flight than in animals used in the synchronous ground-based experiment and animals exposed to artificial gravity during the flight. These data warrant the belief that expressly weightlessness is responsible for development of lymphoid tissue hypoplasia. Thus, the hypoplasia of the thymus observed in rats sacrificed several hours after the space flight is the result of chronic stress, the etiological factor of which is weightlessness.

In addition to lymphoid tissue hypoplasia, we consistently demonstrated inhibition of erythroid hemopoisis in the spleen of rats submitted to weightlessness, as well as accumulation of hemosiderin in it (as a result of intensive disintegration of lymphocytes). As shown by the model experiment, these changes are also observed in hypokinetic animals. Thus, the insufficient muscular activity, which is inevitable as a result of restricted motor activity and weightlessness, is the cause of depressed erythropoiesis in the spleen of rats aboard biosatellites.

According to this study, the "accidental" [sic] involution of lymph organs observed in rats after long-term space flights is the consequence of two stresses, chronic and acute. Chronic stress arises in weightlessness and leads to hypoplasia of lymphoid tissue. Acute stress develops when the animals change from a state of weightlessness to earth's gravity ("gravity stress") and is associated with disintegration of lymphocytes in lymph organs, which aggravates substantially the hypoplasia of lymphoid tissue that appears under the influence of chronic stress due to weightlessness.

BIBLIOGRAPHY

1. Durnova, G. N.; Kaplansky, A. S.; and Portugalov, V. V. AVIAT. SPACE ENVIRONM. MED., Vol 47, 1976, pp 588-591.

2. Durnova, G. N.; Kaplanskiy, A. S.; and Portugalov, V. V. KOSMICHESKAYA BIOL., No 2, 1977, pp 53-57.

3. Idem, ARKH. ANAT. [Archives of Anatomy], No 5, 1977, pp 14-20.

4. Kvetnansky, R., and Mikulaj, L. ENDOCRINOLOGY, Vol 87, 1970, pp 738-743.

5. Kvetnansky, R.; Weise, V. K.; and Kopin, I. J. Ibid, pp 744-749.

6. Genin, A. M., and Sorokin, P. A. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 13, 1969, pp 9-16.

7. Parin, V. V., and Krupina, T. N. in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii" [Adaptation to Muscular Activity and Hypokinesia], Novosibirsk, 1970, pp 134-136.

8. Kovalenko, Ye. A. KOSMICHESKAYA BIOL., No 4, 1977, pp 3-9.

9. Roskin, G. I., and Levinson, L. B. "Microscope Techniques," Moscow, 3d ed., 1957, p 424.

10. Selye, H. BRIT. J. EXP. PATH., Vol 17, 1936, pp 234-248.

11. Idem, "Essays on the Adaptation Syndrome," Moscow, 1960.

12. Gorizontov, P. D. VESTN. AMN SSSR [Vestnik of the USSR Academy of Medical Sciences], No 8, 1976, pp 81-89.

13. Portugalov, V. V.; Kaplanskiy, A. S.; and Durnova, G. N. VESTN. AMN SSSR, No 10, 1971, pp 29-34.

14. Legen'kov, V. I.; Kiselev, R. K.; Gudim, V. I.; et al. KOSMICHESKAYA BIOL., No 6, 1977, pp 3-12.

15. Zimin, Yu. I. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 6, 1971, pp 21-22.

16. Ernstrom, U., and Sandberg, G. ACTA PATH. MICROBIOL. SCAND., Vol 76, 1969, pp 52-60.

17. Sandberg, G. "On the Release of Lymphocytes From the Spleen," Stockholm, 1972.

18. Kotovskaya, A. R.; Vartbaronov, R. A.; and Simpura, S. F. in "Problemy kosmicheskoy biologii," Moscow, Vol 13, 1969, pp 240-247.

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EFFECT OF HIGH AMBIENT TEMPERATURE ON HUMAN PERFORMANCE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 35-38

[Article by A. N. Azhayev, V. I. Zorile and A. N. Kol'tsov, submitted 6 Oct 78]

[English abstract from source]

Mental and physical capacity of men exposed to 30–35° at low humidity and to 25–30° at high humidity remained unaltered. The capacity of men exposed to 40–55°C at 10–25% of relative humidity and to 35–40°C at 85% of relative humidity declined.

[Text] Workers in some occupations have to work at high ambient temperatures. It has been established that overheating has an adverse effect on functional systems of the body [1, 2]. However, the state of human performance [fitness for work, efficiency] when exposed for a long time to high temperatures inducing different degrees of overheating has not been adequately studied [3-6].

Our objective here was to determine the direction and severity of changes in physical and mental fitness of man in the course of many hours of exposure to high temperatures at low and high air humidity.

Methods

Two series of studies were conducted in a thermal vacuum chamber. In the first series, the air and wall temperature constituted 30, 35, 40, 45, 50 and 55°C and relative humidity was 10-25%; in the second series, the levels were 25, 30, 35 and 40°C, and 85%, respectively. The velocity of air movement in the chamber constituted 0.1-0.2 m/s. The tests of the first series lasted 6, 4.2 and 2.3 h at temperatures of 30-45, 50 and 55°C, respectively; in the second series they lasted 6 and 2 h at temperatures of 25-35 and 40°C.

With temperatures of 50 and 55°C and low air humidity, as well as 40°C at high humidity, the tests continued until rectal temperature rose to 38.4°C.

The subjects wore cotton T-shirts, shorts, a cotton fabric work-out suit, socks and shoes.

In all, we conducted 166 tests involving 17 essentially healthy males ranging in age from 24 to 40 years.

The studies were conducted in the fall and winter. Before starting the study, we trained the subjects in performing the tests until relatively stable results were obtained.

At the start of each hour of exposure to high temperature, we measured skin and body (rectal) temperature, heart rate (at rest and with measured exercise), time of simple sensorimotor reaction to a sonic stimulus, muscular strength and endurance of the hands according to the level of residual exertion after the liquid dynamometer held at the level of one-half the maximum muscular exertion for 1 min. Mental fitness was determined by the results of addition and substraction of numbers at a specified rate. In addition, we evaluated quality of control in the mode of compensatory tracking on a TUZO-3 instrument [7], in which the PSP-48 blind landing instrument served as a visual indicator. In the studies, we used sinusoidal input signals at a frequency of 0.1-0.15 Hz. The quality of control was assessed on the basis of determination of equivalent error by adding the values of different levels of errors for each 5 min of continuous work. In addition, the subjects performed standard flight assignments on a flight simulator. The quality of performance on the simulator was checked 4-5 times within 5-6 h. The subjects were exposed to an air temperature of 60°C for 40-60 min prior to each period of work on the simulator in order to maintain overheating conditions (rectal temperature of 38°C). We also determined the reserve capabilities of the subjects with regard to reception and processing of additional information and performance of motor acts on this basis. For this purpose, during the control process (main work), the subjects performed an additional motor task (depression of button) for 1 min in response to presentation of visual green and red signals, and we recorded the latency period of the motor reaction ("time of reaction involving choice").

We conducted 10 additional tests (with the participation of 5 people exposed to a temperature of 55°C), in which a suit was used that provided for water cooling of the entire body surface, with the exception of the face, hands and feet.

Results and Discussion

The results of the first series of tests revealed that there was no appreciable change in well-being of the subjects at ambient temperatures of 30 and 35°C. We only observed some facial hyperemia and wetness of the integument. Under these conditions, there was no substantial change in quality of performance of psychophysiological tests (time of simple sensorimotor reaction and time of reaction with choice), tracking, solving arithmetic problems, as well as muscular force. At a temperature of 40°C, marked perspiration was already noted after spending 1 h in the chamber. Some subjects were listless and sleepy. At the tend of the tests, body temperature was 37.9±0.09°C. Upon further elevation of ambient temperature, there was an increase in perspiration, and it became profuse at 45°C. The sensation of listlessness, unwillingness to work and move was observed in most cases after spending 1 h in the chamber. Many subjects felt febrile in the 3d-4th h. Body temperature reached 38.2-0.15°C in the 6th h in the chamber.

There was reliable deterioration of fitness parameters with exposure to temperatures of 40-45°C. Maximum muscular strength diminished by 20% and tracking quality by 11.7-19.3%. There was a 19-27% increase in number of mistakes made in arithmetic problems. The latency period of response to green and red light signals increased by 17 ms ($P<0.05$) after spending 2 h in the chamber at a temperature of 45°C. After 4 h of exposure to the same temperature, there was also a statistically reliable increase in number of wrong reactions (by 66.6%). Under these conditions, there was no reliable change in time of simple sensorimotor reaction to a sonic stimulus.

At temperatures of 50-55°C, the subjects reported pulsation and pressure in the temples, heavy-headedness after spending 1 h in the chamber. This was associated with elevation of body temperature to 38.5±0.1°C. Maximum changes in muscular strength quality of tracking and solving arithmetic problems at temperatures of 50 and 55°C were observed in the 4th and 2d h, respectively, spent in the chamber. It should be noted that the change in tracking quality did not occur at the very start of control, but some time after beginning to work continuously, in the 3d-4th min.

Performance of measured physical exercise under overheating conditions led to significant increase in heart rate. Thus, we demonstrated an increase in heart rate by 20, 32 and 34/min at ambient temperatures of 45, 50 and 55°C, respectively. At the same temperatures, there was significant decrease in muscular strength following a static physical load.

There was virtually no change in quality of piloting the simulator after exposure to a temperature of 60°C (for 40-60 min). We merely observed some delay in executing the most difficult flight elements (simultaneously holding the specified bank and vertical speed, etc.).

The results of the second series of tests, which were conducted at a high level of air humidity, revealed that the well-being of the subjects was satisfactory at temperatures of 25 and 30°C. Body temperature constituted 37.3±0.06 and 37.5±0.05°C, respectively. We failed to demonstrate a reliable decrease in psychomotor reactions, muscle strength, quality of tracking and solving arithmetic problems.

At the very start of exposure to a temperature of 35°C, all of the subjects developed a feeling of listlessness, unwillingness to work or move. After spending 3 h in the chamber, there was a substantial deterioration of control quality in the tracking mode. Perspiration was profuse. In the 4th-5th h in the chamber, the subjects reported headache, sensation of pressure in the temples and occiput. Body temperature rose to 38.0±0.06°C. With further elevation of ambient temperature (to 40°C), these complaints were presented sooner, in the 2d h in the chamber. The subjects reported a febrile sensation, palpitations, paresthesia of the limbs and head region. Body temperature constituted up to 38.4±0.18°C. Considerable will power had to be applied to perform the work, and there was usually worsening of general well-being, intensification of perspiration, appearance of headache and sensation of pulsation in the temples. A change in work mode (subtraction of numbers projected on a screen instead of tracking) at temperatures of 35 and 40°C was associated with an increase in number of mistakes. At these temperatures, there was a reliable decrease in muscle strength.

Use of a water-cooled suit, in which the water temperature in the vinyl chloride tubing was held at 28-30°C, helped retain comfortable temperature conditions, high physical and mental fitness at ambient temperature of 55°C for the entire test period (4 h).

A comparative analysis of the changes in psychophysiological functions and subjective sensations revealed that fitness under the tested conditions depended not only on the external temperature, but duration of exposure to it and, consequently, degree of overheating of the body. At the start of exposure to high temperatures (after 15-20 min), there was some brief improvement of performance by the subjects, and this apparently occurs as a result of prevalence of excitatory processes and enlistment of adaptive capabilities of the body. Under the same conditions, not infrequently we observed some drop of rectal temperature (by 0.2-0.5°C). With increase in time of exposure to high temperatures and overheating, there was destabilization of piloting skills and decrease in efficiency. The studied parameters of psychophysiological functions did not change reliably in most cases.

Thus, the results of these studies revealed that exposure to ambient temperatures of 30-35°C at low air humidity and to 25-30°C at high humidity does not have an appreciable influence on thermal state, physical and mental fitness of man when performing light physical work involving energy expenditure of 70-100 W/m^2 (operator work). In such cases, the observed functional changes were indicative of the fact that man can adapt to such conditions. According to the classification of human heat states, the above microclimate conditions induce grade I overheating of the body (rectal temperature 37.6°C) and they are considered permissible [8].

At ambient temperatures of 40-55°C and humidity of 10-25%, as well as 35-40°C and 85% humidity, the changes in thermal state and performance were not indicative of adaptation to these conditions. According to the classification of thermal states of man, these temperatures induce grade II overheating (rectal temperature 37.7-38.4°C) and they are considered to be at the maximum permissible level. In order to avoid disruption of adaptive mechanisms of heat regulation, they can be allowed for a limited time, with constant monitoring of functional state of the body's psychophysiological systems.

BIBLIOGRAPHY

1. Gazenko, T. G. ZDRAVOOKHR. TADZHIKISTANA [Tadzhikistan Public Health], Vol 1, No 1, 1933, pp 122-133.

2. Shepelev, Ye. Ya. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1970, pp 44-48.

3. Yeremin, A. V.; Kopanev, V. I.; Azhayev, A. N.; et al. in "Problemy kosmicheskoy meditsiny" [Problems of Space Medicine], Moscow, 1966, pp 166-167.

4. Krutova, Ye. M. Ibid, pp 232-233.

5. Kramarenko, I. B. in "Fiziologiya truda" [Physiology of Labor], Moscow, 1967, pp 173-174.

6. Colquhoun, W. P. AEROSPACE MED., Vol 40, 1969, pp 413-417.

7. Zorile, V. I.; Knyazhinskiy, A. Ye.; and Chichnev, A. Ye. in "Metodika i apparatura dlya issledovaniya psikhofiziologicheskikh kharakteristik cheloveka-operatora" [Methods and Equipment for Testing Psychophysiological Characteristics of Operators], Moscow, 1977, pp 20-25.

8. Azhayev, A. N. in "Aviatsionnaya i kosmicheskaya meditsina" [Aviation and Space Medicine], Moscow, Vol 1, 1969, pp 5-10.

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DYNAMICS OF HUMAN EXTERNAL RESPIRATION AND BLOOD GASES UNDER THE COMBINED EFFECT OF HYPERCAPNIA AND HYPOXIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 38-41

[Article by L. Kh. Bragin, A. Ye. Severin, N. A. Agadzhanyan, G. A. Davydov and Yu. A. Spasskiy, submitted 6 Feb 79]

[English abstract from source]

In manned experiments gas mixtures with a step-by-step increasing pCO_2 and hypoxia of different levels were used. The experiments demonstrated variations in respiration, buffer systems and gases of the blood. The studies emphasized an important physiological role of a constant pCO_2 in blood, when breathing gas mixtures with a different O_2 content.

[Text] Both Soviet and foreign authors have mentioned the influence of hypoxia as a corrective agent to eliminate deconditioning, which occurs when man reduces his motor activity [1-3].

At the same time, it was shown that there is an increase in functional strain of the respiratory system with increase in level of hypoxia. Intensification of pulmonary ventilation causes a substantial drop of partial carbon dioxide tension in alveolar air and circulating blood which, in turn, has a "restraining effect" on intensity of ventilation required to maintain the p_AO_2 level [4].

It was suggested that CO_2 be added to inhaled air in order to reduce hypocapnia and, consequently, to also reduce the symptoms of acute hypoxia [5, 6].

However, it was subsequently demonstrated that addition of CO_2 to rarefied air to a state of normocapnia, with retention of the same partial oxygen tension in the alveoli, induced intensification of altitude sickness symptoms [7].

We submit here the results of studies of dynamics of external respiration, blood O_2 and CO_2 tension with different levels of hypoxia and "staggered" [step-by-step] increase in hypercapnia against the background of hypoxia.

Methods

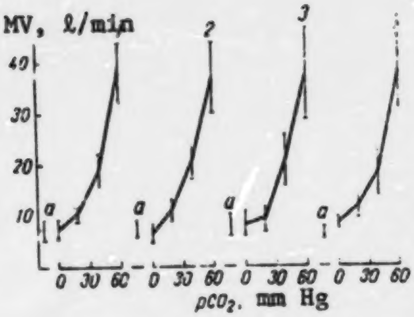
We conducted 4 series of studies with different gas mixtures at normal atmospheric pressure. In the first series, pO_2 of inhaled gas mixtures constituted 160 mm Hg, in the second, third and fourth it constituted 130, 100 and 70 mm Hg, respectively. We added CO_2 to each of these mixtures. The conditions of our tests involved elevation of pCO_2 in the inhaled mixture every 15 min, from 0 to 19, 38 and 57 mm Hg. In the 13th-15th min of breathing each of these hypercapnic-hypoxic mixtures, we measured the pulse rate, arterial pressure, P_aCO_2, P_aO_2, pH, respiratory quotient, CO_2 output, O_2 uptake, respiratory rate, minute volume (MV) of respiration. Exhaled air was collected in rubberized bags. We took an air sample from each bag and submitted it to analysis on an Ors-Fisher gas analyzer. We used a micro-Astrup instrument to measure pH and buffer components of blood, P_aO_2 and P_aCO_2. The other parameters were determined by the estimation method. In each series of studies there were eight participants. In all, we conducted 32 tests. The obtained data were submitted to statistical processing according to Student.

Results and Discussion

When breathing air, the respiratory rate of the subjects was 13-15/min, and it did not change appreciable with the change to a gas mixture with pO_2 of 160 to 70 mm Hg. Addition of CO_2 to the inhaled gas mixtures in an amount, with which pCO_2 constituted 19 mm Hg, did not induce an appreciable increase in rate of respiration. With pCO_2 of 38 mm Hg, the respiratory rate increased to 14-18/min, but this increase was also unreliable. It is only with inhalation of gas mixtures with pCO_2 of 57 mm Hg that there was a reliable ($P<0.05$) increase in respiratory rate to 18-23/min. The change from breathing air to breathing a hypoxic mixture with pO_2 of 70 mm Hg was associated with a statistically marked increase in pulmonary ventilation ($P<0.05$), which is consistent with the findings of a number of authors [8].

A comparison of pulmonary ventilation volume in subjects of all series of studies revealed that its mean level with the same degree of hypercapnia was quite similar, in spite of the different pO_2 levels in the mixtures. With pCO_2 of 19 mm Hg, pulmonary ventilation constituted 10-11 ℓ/min in all of the series. Elevation of pCO_2 in the inhaled gas mixtures to 38 mm Hg induced a reliable increase in MV, which increased to 18-20 ℓ/min BTPS at all pO_2 levels.

We demonstrated a correlation between pulmonary ventilation and degree of hypercapnia, while the presence of a "hypoxic component" in the pO_2 and pCO_2 combinations we used did not have a statistically marked effect on MV (see Figure).



MV with staggered elevation of pCO_2 against the background of different p) levels in inhaled air.
a) respiration of atmospheric air
1-4) pO_2 of 160, 130, 100 and 70 mm Hg, respectively

In all of the series of tests, there as an increase in O_2 uptake with elevation of pCO_2 in the inhaled gas mixtures to 57 mm Hg, but this was reliable only in the first series, where it constituted 344 40 mℓ/min STPD.

With such brief exposure to the gas environment, this probably occurs as a result of increased oxygen requirement due to the increase in energy expended on breathing and release of catecholamines in response to the "stressor" effect of CO_2, as well as because of the increase in $PaCO_2$ which is instrumental in output of O_2 as a result of a right shift of the curve of oxyhemoglobin dissociation (Bohr effect).

Ouput of CO_2 while breathing the same mixtures manifested, on the contrary, a tendency toward decrease. With pCO_2 of 57 mm Hg, CO_2 output dropped to 106-142 mℓ/min STPD. The respiratory quotient dropped to 0.5-0.72. The decline of the respiratory quotient when breathing mixtures with high CO_2 and low pO_2 is indicative of impaired stability of the correlation between CO_2 output and O_2 uptake.

Evidently, we can refer here to the effect of "locking" of endogenous CO_2 by exogenous CO_2 [9], as well as CO_2 binding (or more precisely binding of the HCO_3^- ion) by tissues [10].

In all series of studies, pCO_2 and pO_2 of peripheral blood underwent substantial change. P_aO_2 decreased, and the greater the O_2 shortage in inhaled air the more significant this decrease under the influence of hypoxia. In the fourth series, O_2 tension in blood dropped from 87 to 41 mm Hg. Addition of CO_2 to the mixtures increased pO_2 of blood. In the first series of studies, it rose to 93 mm Hg, i.e., it was 10 mm Hg higher than the initial level. In the second series, O_2 tension of blood showed virtually no difference from base levels (inhaling atmospheric air) with inhalation of a gas mixture with pO_2 or 130 mm Hg and pCO_2 of 57 mm Hg. In the third and fourth series, P_aO_2 rose by 20 mm Hg, but still was below base levels (due to the significant degree of hypoxia), constituting 77 and 61 mm Hg, respectively.

When breathing gas mixtures, blood CO_2 tension also presented typical dynamics. With pO_2 of 100 and 70 mm Hg, P_aCO_2 dropped from 39 to 36 and to 29 mm Hg, respectively. Addition of CO_2 to the gas mixtures, to 57 mm Hg, increased blood CO_2 tension by 17-21 mm Hg, constituting 59, 55, 53 and 51 mm Hg in the first to fourth series, respectively.

A comparison of the data shows that only inhalation of a gas mixture with pO_2 of 70 mm Hg and pCO_2 of 0 mm Hg induced a substantial decline of P_aCO_2 as compared to initial levels. Addition of CO_2 to the inhaled gas mixture to a partial pressure of 19 mm Hg did not lead to a change in P_aCO_2 as compared to the initial level (breathing atmospheric air). Elevation of pCO to 38 mm Hg led to an increase in P_aCO_2, which was reliable only with pO_2 of 100 mm Hg in the inhaled gas mixture.

Finally, with pCO_2 of 57 mm Hg, we observed substantial saturation of peripheral blood with CO_2 at all levels of oxygen delivery to the body. Accumulation of CO_2 in the body and elevation of blood CO_2 tension induced about the same increase in blood acidity in all of the study series. pH constituted 7.33-7.35. There were also consistent dynamics to the buffer components of blood. The concentration of total bases had a tendency toward decrease in all series of studies: from 57.3-52 in the base state to 53.5-50 meq/ℓ when breathing gas mixtures where pCO_2 was 57 mm Hg. The concentration of actual bicarbonates decreased substantially, to 17.4-13.9 meq/ℓ, only when breathing gas mixtures with partial CO_2 pressure of 57 mm Hg; we failed to demonstrate any correlation between this and level of hypoxia.

There was a tendency toward decrease in amount of bicarbonates when scaled to standard conditions.

Finally, the index of compensation of CO_2 excess by buffer systems of blood ("base shortage") remained virtually unchanged in the first and second series, whereas in the third there was a reliable drop when breathing mixtures with pCO_2 of 38 and 57 mm Hg, to 1.4 and 0.5 meq/ℓ, respectively (versus the base level of 3.1 meq/ℓ). In the fourth series, we also observed a tendency toward decline of this parameter with increase in pCO_2 of inhaled gas mixtures, but only with the use of a gas mixture with pCO_2 of 57 mm Hg did this decline become reliable: from 3 meq/ℓ in the initial state to 1.12 meq/ℓ when breathing the above mixture. However, this decline should be deemed moderate, and it is indicative of the presence of respiratory acidosis with no signs of metabolic acidosis.

Thus, the dynamics of parameters of external respiration, blood buffer systems and gases when man is exposed to staggered levels of hypercapnia against the background of different levels of hypoxia are indicative of the need to take into consideration the important physiological role of a constant blood pCO_2 level when breathing gas mixtures containing different amounts of O_2.

BIBLIOGRAPHY

1. Genin, A. M. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 3, 1964, pp 59-65.

2. Agadzhanyan, N. A. "Physiological Substantiation of General Pressure and Oxygen Levels in the Cabins of Aircraft," author abstract of doctoral dissertation, Moscow, 1968.

3. Lamb, L. E., et al. AEROSPACE MED., Vol 35, 1964, pp 420-429.

4. Agadzhanyan, N. A.; Davydov, G. A.; and Spasskiy, Yu. A. FIZIOLOGIYA CHELOVEKA [Human Physiology], Vol 3, No 2, 1977, pp 343-344.

5. Strel'tsov, V. V. in "Voprosy aviatsionnoy meditsiny" [Problems of Aviation Medicine], Moscow, 1938, pp 60-80.

6. Strumza, M. V. AEROSPACE MED., Vol 36, 1965, pp 850-854.

7. Maher, J. T.; Cymerman, A.; Reeves, J. T.; et al. AVIAT. SPACE ENVIRONM. MED., Vol 46, 1975, pp 826-829.

8. Malkin, V. B., and Gippenreyter, Ye. B. "Problemy kosmicheskoy Biologii," Moscow, Vol 35, 1977, p 69.

9. Nizovtsev, V. P. "Latent Respiratory Insufficiency and Simulation Thereof," Moscow, 1978, pp 145-147.

10. Skulkova, N. P. "External Respiration, Gas Exchange and Parameters of Gas Composition of Arterial and Venous Blood in Experimental Hypercapnia," author abstract of candidatorial dissertation, Kuybyshev, 1974.

UDC: 612.176

FUNCTIONAL STATE OF THE CARDIOVASCULAR SYSTEM UNDER THE COMBINED EFFECT OF 28-DAY IMMERSION, ROTATION ON A SHORT-ARM CENTRIFUGE AND EXERCISE ON A BICYCLE ERGOMETER

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by I. F. Vil'-Vil'yams and Ye. B. Shul'zhenko, submitted 19 Nov 78]

[English abstract from source]

The cardiovascular function of four test subjects exposed to 28-day "dry" immersion was examined before and after 6-day cycles of rotation in a short-arm centrifuge to provide 1 2 G_z, bicycle ergometer exercise, and their combination. An exposure to acceleration of 3 G_z in a 7.25 m arm centrifuge was used as a provocative test. The above countermeasures reduced but not eliminated entirely immersion-induced cardiovascular deconditioning. From this study a combined use of acceleration of 1 -2 G_z in a short-arm centrifuge and bicycle ergometer exercise can be recommended as a countermeasure against cardiovascular deconditioning in weightlessness.

[Text] Rotating man on a short-arm centrifuge (SAC) is one of the possible means of preventing the effects of deconditioning in weightlessness [1-3].

Our objective here was to assess the functional state of the circulatory system and endurance of $+G_z$ accelerations after long-term exposure to "head-pelvis" accelerations in the range of 1-2 G on a SAC and exercise on a bicycle ergometer under conditions simulating the effects of weightlessness by means of immersion.

Methods

Four studies were conducted on healthy male volunteers involving 28-day immersion, based on the principle of "wet" submersion using highly elastic water-proof material [4]. The water temperature in the tank constituted 34±0.5°C, i.e., it was thermally neutral [5]. We used SAC rotation at different stages of immersion (see Table) in a progressively increasing mode. For 6 days, they were exposed for 2 days to each of the following levels of acceleration: +0.8, 1.2 and 1.6 Gz (at foot level) lasting 60 min at a time, twice a day. The resulting G forces constituted 1.3, 1.6 and 1.9, respectively.

Schedule of tests during 28-day immersion

Day of immersion	SAC	Bicycle ergometer	Centrifuge with 7.25-m arm
Before immersion	--	—	+
1st-7th	—	—	—
8th	—	—	+
9th-14th	+	—	—
15th	—	—	+
16th-21st	—	+	—
22d	—	—	+
23d-28th	+	+	—
After immersion	—	—	+

The exercise on the bicycle ergometer involved a load of 600 kgf/min with 10 min of pedaling and 10 min of rest (3 such cycles for 60 min twice a day). In all, there were 96 rotations on the SAC, 48 of which were combined with pedaling. There were also 48 sessions of exercise on the bicycle ergometer that were not combined with rotation on the SAC. We generated +3Gz with an increment gradient of 0.2 G/s before immersion (7 days before), on the 7th, 14th, 21st and 28th days of immersion as a functional load test using a centrifuge with a 7.25-m arm. Rotation lasted up to 5 min before immersion, on the 7th and 28th days of immersion, and 1 min on the 14th and 21st days. We recorded the electrocardiogram (EKG) in the leads of (Neb) and arterial pressure (AP) in vessels of the ear lobe as modified in [6].

We recorded the EKG lead in the Neb leads, phonocardiogram, sphygmogram of the carotid artery, rheogram of the femoral artery using a 4RG-1A instrument, AP of the brachial artery using an AP-KTs instrument (Biofizpribor Plant) and elasticity of venous vessels of the arm by the method in [7] as modified in [8], before and after each preventive cycle. We calculated the heart rate (HR), systolic (SV) and minute (MV) volumes of the heart by the method of Bremzer-Ranke, and total peripheral resistance (TPR) using the formula of Poiseuille.

All of the data were submitted to variational processing according to Student. The differences were considered reliable with $P<0.05$.

Results and Discussion

There were phasic changes in mean parameters of systemic circulation during immersion (Figure 1). The most marked changes (usually within 10-20% of initial levels) were noted after 7 days of "pure" immersion, and they were typical of the hypodynamia syndrome[9]: decreased SV and MV (from 93 to 82 mℓ and from 5.8 to 5.0 ℓ/min, respectively), increased TPR (from 1138 to 1512 dynes/s/cm^{-5}), elevation of diastolic AP (from 63 to 76 mm Hg) and drop of pulse AP (from 44 to 35 mm Hg). By the 14th day of immersion, HR decreased by 5/min. There was a tendency toward restoration of the main hemodynamic parameters to the base level under the influence of the preventive measures. On the 28th day of immersion, this tendency was significant for SV and pulse AP, as compared to the 7th day.

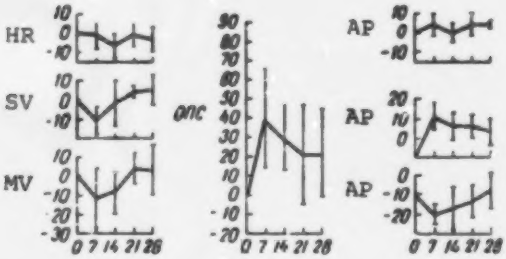

Figure 1.
Dynamics of relative changes in parameters of the cardiovascular system during 28-day immersion. X-axis, days of immersion; y-axis, parameters of cardiovascular system (Δ% of base levels)

There was significant increase in elasticity of vessels of the arm during immersion, which was indicative of substantial decrease in tonus of venous vessels (Figure 2). The changes in these parameters were the most marked (about 4-fold, as compared to the initial level) also on the 7th day of immersion.

The degree of change in mean values of parameters characterizing venous tonus diminished under the influence of preventive measures, although these changes were not usually statistically significant.

Endurance of +3Gz accelerations constituted a mean of 298±2 s for the entire group. After 7 days of "pure" immersion there was an overt tendency toward decrease in endurance to 130±87 s. Impaired vision in the form of a "gray" film or drop of AP in vessels of the ear lobe to below 40 mm Hg were the chief symptoms limiting endurance of G forces. On the 15th and 22d days of immersion after using preventive measures, all of the subjects endured 1 min of scheduled exposure to +3 Gz. Duration of final exposure to G forces after immersion for 28 days constituted 273±50 s, and it did not differ reliably from the duration of control rotations, which is indicative of diminished functional reserves of the circulatory system under the influence of the set of preventive measures.

A comparison of cardiovascular reactions to +3 Gz accelerations before and after 28-day immersion revealed that the postimmersion changes were more marked: increased synus tachycardia, drop of AP of ear lobe vessels, although it constituted a mean of 60 mm Hg in the 5th min of rotation, and it was above critical levels (Figure 3).

Thus, use of periodic rotation on the SAC (in the range of 1-2 G lasting for up to 60 min twice a day) combined with exercise on a bicycle ergometer

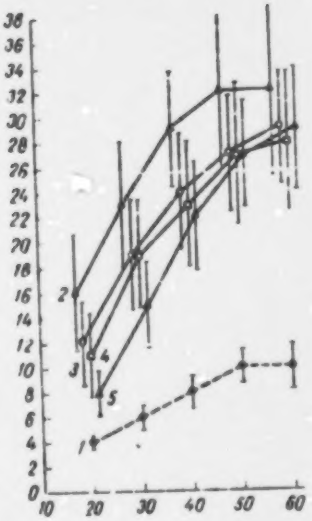

Figure 2.
Dynamics of elasticity of arm vessels during 28-day immersion. X-axis, pressure in cuff applied over arm (mm Hg) x-axis, elasticity of vessels of the forearm (in arbitrary units)

1) before immersion
2-5) 7th, 14th, 21st and 28th days of immersion, respectively

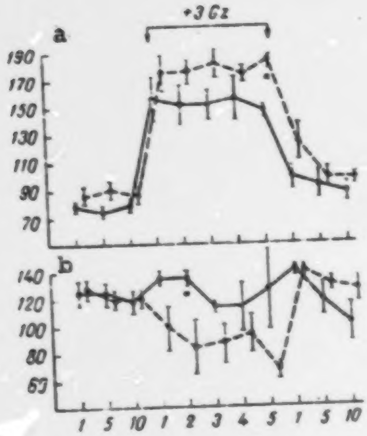

Figure 3.
Dvnamics of parameters of the cardiovascular system with exposure to +3 Gz accelerations lasting for 5 min before and after 28-day immersion. X-axis, time of exposure (min); y-axis: a--HR (per min); b--AP in vessels of ear lobe. Asterisk indicates $P<0.05$ when comparing parameters before (solid line) and after (dash line) immersion

attenuated the effects of deconditioning of the cardiovascular system caused by prolonged immersion. These results are consistent with those of previous studies of preventive effects of periodic "gravity" loads at low levels simulated on a centrifuge with a medium-sized arm [1].

The preventive effect of the "gravity" loads combined with exercise on a bicycle ergometer was probably attributable to the complex influence of a number of factors, in particular, simulation of the hydrostatic blood pressure gradient along the great vessels of the body and simulation of a load on the skeletomuscular system. As we know, this stimulates mechanisms that regulate vascular tonus and attenuates signs of atrophy of the main antigravity skeletal muscles "due to disuse" [10]. Evidently, the increased expenditure of energy related to exercise was also important, and perhaps it had some influence on MV dynamics during immersion in view of the close correlation between these parameters [11]. Probably, the function of the peripheral muscle pump while pedaling on the bicycle ergometer also played a role; this, as we know, is involved in increasing venous return of blood to the heart and when associated with exposure to low levels of +Gz accelerations and the magnitude of exercise we selected (600 kgf/min) increases venous return to the heart, cardiac output and pulmonary flow, and has a tonic effect on the cardiovascular system [12].

These studies also revealed that the effects of deconditioning of the cardiovascular system under the influence of the tested preventive measures were not completely eliminated. As can be seen from our findings, diminished tonus of capacitance vessels, which was perhaps related to decreased tonus of the adrenosympathetic and muscular systems during immersion, may be one of the possible causes of this phenomenon [13].

The obtained data warrant recommendation of the combination of rotation on a SAC in the range of 1-2 G and physical exercise on a bicycle ergometer as a means of preventing deconditioning of the cardiovascular system when in weightlessness.

BIBLIOGRAPHY

1. Shul'zhenko, Ye. B. "Physiological Effects of Altered Gravity (Model Experiments on the Ground)," author abstract of doctoral dissertation, Moscow, 1975.
2. Burnazyan, A. I.; Vorob'yev, Ye. I.; Gazenko, O. G.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1977, pp 3-12.
3. Kotovskaya, A. R.; Galle, R. R.; and Shipov, A. A. Ibid, No 2, pp 12-19.
4. Shul'zhenko, Ye. B., and Vil'-Vil'yams, I. F. Ibid, No 2, 1976, pp 82-84.
5. Craig, A. B., and Dvorac, A. B. J. APPL. PHYSIOL., Vol 21, 1966, pp 1577-1585.
6. Suvorov, P. M. "Physiological Studies on a Centrifuge in the Practice of Medical Flight Certification and Screening System," author abstract of doctoral dissertation, Moscow, 1969.
7. Newberry, P. D., and Bryan, A. C. J. APPL. PHYSIOL., Vol 23, 1967, pp 150-156.
8. Webb, P. in "Hypogravic and Hypodynamic Environments. A. Symposium Held at French Lick," Indiana University, 1969, pp 395-409.
9. Genin, A. M., and Sorokin, P. A. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 13, 1969, pp 9-16.

10. Genin, A. M., and Pestov, I. D. in "Chelovek v Kosmose. Mezhdunarodnyy simpozium po osnovnym problemam zhizni cheloveka v kosmicheskom prostranstve, 4-y, Trudy" [Man in Space. Proceedings of 4th International Symposium on the Chief Problems of Human Life in Space], Moscow, 1974, pp 76-87.

11. Guyton, A. "Physiology of Circulation. Minute Volume of the Heart and Regulation Thereof," Moscow, 1969.

12. Nunneley, S. A., and Shindell, D. S. AVIAT. SPACE ENVIRONM. MED., Vol 46, 1975, pp 878-882.

13. Gauer, O. H. in "Chelovek v Kosmose. Mezhdunarodnyy simpozium po osnovnym problemam zhizni cheloveka v kosmicheskom prostranstve, 4-y, Trudy," Moscow, 1974, pp 176-191.

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PHARMACOLOGICAL ANALYSIS OF PHYSIOLOGICAL MECHANISMS OF ORTHOSTATIC HEMODYNAMIC STABILITY

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[Article by L. I. Osadchiy, submitted 30 Jan 78]

[English abstract from source]

In urethane anesthesized cats, securinine brought about a distinct increase in compensatory reactions of arterial pressure and cardiac output during an upright tilt at 45°. The experiments also showed a substantial increase in compensatory recovery of the volume velocity of circulation in the posterior vena cava. Myorelaxant induced arrest of contractile function of skeletal muscles prior to securinine administration reversed compensatory reactions of arterial pressure and cardiac output during tilt test.

[Text] The increased interest in recent years in questions of stability and gravity loads is related to the need to develop preventive measures to lower the intensity of reactions when changing from weightlessness to earth's gravity. This also applies to gravity loads with orthostatic reactions that occur after spending a long time in horizontal position without exercise. The existing facts indicate that there is a possibility of preventing hemodynamic orthostatic reactions following hypodynamia by means of pharmacological agents that stimulate the central nervous system [1] and circulatory system [2].

On the other hand, there are data pertaining to adaptive reactions of the circulatory system to orthostatic factors [3-6]. It was previously established [5] that compensatory arterial pressure reactions are determined in cats in the orthostatic test chiefly by the vascular component of the systemic reaction to orthostasis. Moreover, it was found that the baroreceptive reflexes, which are of substantial significance to these compensatory reactions, occur mainly by means of change in tonus of peripheral vessels.

In view of the foregoing, it was deemed important to explore the physiological mechanisms at the basis of compensatory hemodynamic reactions to orthostastatic position, which are stimulated by pharmacological agents, in particular securinine, which increases orthostatic stability of man [1]. This product is known as a central nervous system stimulant of plant origin, which has a strychine-like action [7].

Methods

Experiments were conducted on cats under urethan anesthesia (1.0 g/kg). The orthostatic test (OT) was performed by turning the table to 45° from the horizontal axis with the head up for 1-3 min. Arterial pressure (AP) was measured in the carotid artery with a mechanotronic electromanometer [8]. In some experiments, a similar sensor was used to record central venous pressure (CVP) in the anterior vena cava and, through a catheter, in the external jugular vein. The external tips of the catheter were on the pivot shaft [axis of rotation] of the table to avoid artefacts when there was a change in correlation between levels of the catheters and pressure sensors. The cuff sensor of an RKE-1 electromagnetic flowmeter [9] was used for continuous recording of cardiac output; this device records the volumetric blood flow rate in the ascending aorta. Volumetric blood flow rate in the posterior vena cava was recorded with the flow-type sensor of an RKE-1 electromagnetic flowmeter inserted in the vessel that carries blood from the posterior vena cava to the right atrium [10]. All of the processes were recorded on an USChV-8 ink-writing oscillograph, and the data were submitted to statistical processing using Student's paired *t*-test.

Results and Discussion

In the first series (13 experiments) we studied the effect of securinine on systemic hemodynamics in order to determine the range of doses that alter the activity of the cardiovascular system (Table 1).

It was established that, in a dosage of 0.25 mg/kg, securinine elicited reliable pressor changes in AP in only half the cases (out of 26), and it did not affect cardiac output in any case. Such a dosage of securinine may be considered the threshold for the circulatory system. Increase in dosage to 0.5 mg/kg was associated with appearance of pressor reactions in 20 out of 23 cases, as well as reliable increase in cardiac output in the same 20 cases. Further increase in dosage to 1.0 mg/kg led to an increase in amplitude and duration of pressor AP reactions and cardiac output changes in all 16 cases, and this was associated with marked general motor activity of the animal.

It should be noted that, in our experiments, we demonstrated greater sensitivity of the circulatory system to securinine (by about 3-4 times) than in previously published articles [7].

Although we cannot derive a definitive conclusion about the mechanism of action of securinine on systemic hemodynamics on the basis of the reported data, it can be assumed that securinine affects the circulatory system, and its action depends on both its direct influence on vasomotor centers and changes in muscular activity of central origin. It is known that the latter could lead to involvement of the "muscular pump" [10, 11] in the reaction, which expells blood from the veins to the heart and thereby increases cardiac output and AP. Moreover, we cannot rule out the peripheral effect of securinine on smooth muscles of the vascular walls.

Table 1. Changes in AP and cardiac output of cats given different doses of securinine (M±m)

Securinine dose, mg/kg	Number of cases	AP, mm Hg			Cardiac output, mℓ/min		
		base level	Δ_{max}	P	base level	Δ_{max}	P
0,25	13	130	+4,8±1,5	<0,05	310	+12±7,2	<0,05
0,5	20	127	+8,2±1,7	<0,05	288	+22±6,2	<0,01
1,0	16	122	+12,4±2,8	<0,01	272	+32±7,8	<0,01

All of the above mechanisms are directed toward increasing vascular tonus and output of the heart.

In the second series (14 tests) we studied the effect of securinine on compensatory reactions of systemic hemodynamics, which develop in response to a positive gravity load under OT conditions.

It was established that administration of securinine in a dosage of 1.0 mg/kg was associated with reliable change in compensatory reactions of the cardiovascular system in 19 cases (out of 28) (Table 2). While AP dropped by a mean of 20% of the initial level in response to orthostatic conditions and maximum restoration of AP during the OT period reached 25% before giving securinine, after administration of this agent the latter index constituted 70% of the maximum AP decline, which constituted 16% of the base level. Before administration of securinine, cardiac output decreased by a mean of 22% of the base level, while recovery was virtually absent in the OT period; after giving securine, the last mentioned parameter constituted 70% of maximum AP decline, which amounted to 16% of the base level. Before giving securinine, cardiac output dropped by a mean of 22% of the base value, and there was virtually no restoration during the OT; after giving securinine, the maximum decline of cardiac output constituted 16% of the initial level and restoration was 64% of maximum decline of cardiac output.

We recorded volumetric flow rate in the posterior vena cava in seven experiments to define the dynamics of venous return to the heart during OT. We found that, while venous influx, which initially dropped by a mean of 48%, failed to demonstrate a tendency toward compensatory restoration before giving securinine, after the latter it constituted 72% of the maximum decrease in venous influnx in the posterior vena cava. The latter corresponds in phase to the compensatory change in AP and CVP observed in these tests, as well as the compensatory cardiac output reactions demonstrated in the experiments described above.

Table 2. Effect of securinine (1.0 mg/kg) on orthostatic stability of systemic hemodynamics (AP and cardiac output) of cats

Experimental conditions	AP, mm Hg			Cardiac output, mℓ/min		
	base level	Δ_{20}	Δ_{60}	base level	Δ_{20}	Δ_{60}
Before giving securinine	142±12	−28±2,8	−21±3,2	268±18	−59±7,4	−55±6,4
After giving securinine	152±8	−24±4,2	−8±2,5	284±12	−45±6,6	−16±4,2
P	>0,05	>0,05	<0,01	>0,05	>0,05	<0,01

Note: Mean values of 14 tests are given. Δ_{20} and Δ_{60} refer to changes in the 20th and 60th s, respectively, of 3-min OT.

Evidently, the mechanism of restoration of AP during the OT is determined both by intensification of recovery of venous influnx to the heart, which in turn leads to increased cardiac output, and increased vascular tonus. The latter could lead to a greater AP reaction, not only as a result of increase in resistance of resistive vessels, but by virtue of involvement in the compensation process of tonus of capacitive vessels [5, 6, 10], with subsequent increase in CVP and intensification of venous influx to the heart, which leads to an increase in cardiac output.

Consequently, securinine can affect compensatory AP reactions via both mechanisms, cardiac and vascular, and interaction between these factors was confirmed in an analysis of a number of other systemic circulatory reactions [10]. However, in view of the more marked vascular component of systemic reactions to orthostatic position [7], there is every reason to believe that the cardiac output changes are secondary to the primary compensatory changes in vascular tonus.

In view of the strychnine-like central effect of securinine and related increase in motor activity of the animals, we studied the influence of involvement of contractile activity of skeletal muscles on the above-mentioned effect of enhancement of orthostatic stability by securinine.

To rule out contractile activity of muscles, we used the muscle relaxant lysthenon in a dosage of 2 mg/kg, which completely paralyzes skeletal muscles of the limbs and respiratory muscles in the 15th-20th min. Lysthenon was given just prior to securinine (in a dosage of 1.0 mg/kg).

In seven tests (third series), it was demonstrated that, while the maximum compensatory reaction of AP during the OT reached a mean of 28% of the maximum AP drop prior to exclusion of contractile activity of skeletal muscles, 3 min after giving the myorelaxant followed by administration of securinine there was no recovery of AP in any of the tests. As for the cardiac output reaction, securinine did not induce compensatory changes in the case of preadministration of lysthenon, although, as indicated above, this agent stimulated compensatory reactions of both AP and cardiac output.

The obtained findings warrant the conclusion that motor activity of skeletal muscles, which occurs in response to the OT [6], plays a substantial role in the mechanism of maintaining orthostatic stability by enhancing compensatory changes in systemic hemodynamics. Elimination of muscular activity virtually eliminates compensatory influences under orthostatic conditions which were stimulated by securinine. This is probably related primarily to involvement of the "muscle pump," in view of intensification of contractile activity of skeletal muscles.

Thus, it was demonstrated that securinine can have a preventive effect, by enhancing orthostatic stability of the organism. This is consistent with the above data concerning the increase in orthostatic stability after administering securinine to individuals following hypodynamia [1]. The fact that orthostatic stability increased in individuals during many hours of immersion as a result of being given small doses of vasopressin [6] may serve as a confirmation of this. Studies were conducted that established that adrenostimulators increase human stability with the head tilted upward at an angle of 45° [12]. We know of studies that demonstrated an increase in resistance to gravity loads after administration of agents capable of increasing vascular tonus [13].

In conclusion, it should be noted that pharmacological analysis of the mechanisms of orthostatic stability permits demonstration of the physiological mechanisms at the basis of compensatory reactions, which are related to activation of the cardiovascular and muscular systems.

BIBLIOGRAPHY

1. Vasil'yev, P. V., and Lapinskaya, B. Yu. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 13, 1969, pp 206-214.

2. Parin, V. V.; Vasil'yev, P. V.: and Belay, V. Ye. IZV. AN SSSR. SERIYA BIOL. [News of the USSR Academy of Sciences, Biology Series], o 4, 1965, pp 481-490.

3. Katkov, V. Ye. "Dynamics and Regulation of Circulation Under Orthostatic Conditions," author abstract of candidatorial dissertation, Moscow, 1974.

4. Katkov, V. Ye. KARDIOLOGIYA [Cardiology], No 1, 1977, pp 123-127.

5. Osadchiy, L. I. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 12, 1977, pp 650-653.

6. Gauer, O. H., and Thron, H. L. in "Handbook of Physiology," Washington, Sect 2, Vol 3, 1965.

7. Turova, A. D. FARMAKOL. I TOKSIKOL. [Pharmacology and Toxicology], No 4, 1956, pp 11-17.

8. Kornyushkin, Yu. D., and Osadchiy, L. I. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 2, 1964, pp 225-226.

9. Osadchiy, L. I. in "Tsentral'naya regulyatsiya krovoobrashcheniya" [Central Regulation of Circulation], Volgograd, 1977, pp 150-151.

10. Idem, "Cardiac Function and Vascular Tonus," Leningrad, 1975.

11. Guyton, A. "Physiology of Circulation. Minute Volume of the Heart and Regulation Thereof," Moscow, 1969.

12. Nolan, P. L., and Bentley, G. A. CLIN. EXP. PHARMACOL. PHYSIOL., Suppl 2, 1975, pp 213-218.

13. Belay, V. Ye.; Vasil'yev, P. V.; and Glod, G. D. in "Problemy kosmicheskoy biologii," Moscow, Vol 6, 1967, pp 124-136.

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BIOELECTRIC ACTIVITY OF THE HUMAN BRAIN DURING AND AFTER 182-DAY ANTIORTHOSTATIC HYPOKINESIA

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[Article by T. N. Krupina, Kh. Kh. Yarullin and D. A. Alekseyev, submitted 22 Apr 78]

[English abstract from source]

Cerebral bioelectric activity of 18 healthy test subjects, aged 31—40, was examined during and after their 182-day head-down tilting. The test subjects were divided into a group that performed countermeasures (exercise, muscle stimulation) against hypokinesia-induced disorders and a control group. During the study EEG changes were most pronounced in the controls: α-rhythm amplitude, frequency and index decreased, slow wave frequency reduced, whereas index of zonal differences and amplitude of β- and slow waves increased. Phasic changes in the central nervous system excitability in response to a flickering light of 6—25 cps were found. Typical changes in spontaneous EEG during a 3 min pulmonary hyperventilation test were enhanced. The study gives evidence that the dynamics of spontaneous EEG as well as cerebral bioelectric activity in response to flickering light and pulmonary hyperventilation are important indicators of the cerebral function, especially of the cortical activity decrease.

[Text] One of the most pressing problems of space medicine is to preserve a high degree of performance by cosmonauts during exposure to weightlessness for a long time. It is of great practical importance to study the functional state of the central nervous system during long-term space flights and, consequently, prognostic determination of its capabilities and reserves from these standpoints.

Our objective here was to make an electroencephalographic study of the functional state of the human brain during simulation of the physiological effects of weightlessness by means of bed rest in antiorthostatic (-4° tilt of head) position, as well as to assess the efficacy of preventive and rehabilitation measures.

Methods

Studes of 182-day antiorthostatic hypokinesia (ANOH) were conducted on 18 men ranging in age from 31 to 40 years following a thorough clinical examination. We formed 3 groups of subjects with 6 men in each: the first consisted of individuals submitted to ANOH with the use of a physical load involving a total expenditure of energy of about 1800 kcal over a 4-day cycle; the second consisted of men exposed to ANOH with half the physical load of the first group, and the third was a control group. We used lower body negative pressure (LBNP) and fluid-sodium correction as additional preventive measures for the first and second groups. In addition, electric stimulation of the muscles was performed in the first group. The article of L. I. Kakurin et al. [1] provides more details on the set of preventive measures. ANOH conditions are analogous to those described by A. D. Voskresenskiy et al. [2].

The electroencephalogram (EEG) was taken in the background period, 4th, 16th, 32d, 61st, 96th, 128th and 176th days of ANOH, 4th, 15th, 30th and 50th days of the rehabilitation period, from 8 symmetrical points on the scalp (forehead, center, temple, occiput) in bipolar and monopolar variants, on a portable 8-channel electroencephalograph, at rest (spontaneous EEG) and during functional tests (rhythmic photostimulation at a frequency of 6-25 Hz and pulmonary hyperventilation for 3 min). Along with visual evaluation of the EEG of the right central and occipital lead at rest and with hyperventilation, we determined the amplitude, frequency and index of α-, β-, θ- and δ-activity, calculated (in arbitrary units) the index of regional differences (ratio of index of α-rhythm in the right central occipital lead to index of α-activity in the frontocentral lead). These parameters were submitted ot statistical processing using the *t* criterion. The severity of diffuse changes in bioelectric activity of the brain was assessed according to Ye. A. Zhirmunskaya [3]. The sign criterion was used for statistical processing of the results of the test with rhythmic photostimulation [4]. The variants of responses with adoption of rhythm, change therein, depression of main activity and its synchronization were summated separately for two groups of frequencies: 15, 20, 25 and 6, 9, 12 Hz.

Results and Discussion

The spontaneous background EEG was in the normal range in 13 subjects, while mild (1 subject in the second and 1 in the third group), or mild and moderate diffuse changes (3 subjects in the first group) in bioelectric activity of the brain were noted in the rest. In addition, during hyperventilation there were mild diffuse changes lacking in the spontaneous EEG in another 3 subjects of the second group.

Thus, the background studies revealed that the groups were not homogeneous according to EEG parameters. The control group was characterized by the greatest homogeneity and least changes in bioelectric activity of the brain, as compared to the first and second groups. In 5 subjects of the third group, bioelectric activity of the brain was in the normal range, and only 1 subject was an exception: against the background of a "desynchronized" EEG, he presented bursts of high-amplitude (up to 60 µV) β-activity at a frequency of 18 Hz.

Maximum heterogeneity and EEG changes in the background studies were noted in the first group. They consisted of disorganization of α-rhythm and build-up of slow activity during hyperventilation in 2 subjects, and presence of high-amplitude (70 µV, 3 Hz) diffuse, polymorphic σ-activity, as well as diffuse θ-activity (up to 40 µV) against the background of marked disorganization of main rhythm in 1 subject.

In 5 subjects of the second group, the spontaneous EEG was in the normal range, while there was dominance of β-activity (18 Hz, 25 µV and 30 Hz, 50 µV) against the background of disorganized α-activity in 1 subject. Mild and diffuse changes in bioelectric activity of the brain appeared in 3 subjects during hyperventilation.

In the control group, in spite of greater homogeneity and less marked changes in the background EEG, the changes in EEG parameters were found to be the most significant during ANOH. The amplitude of α-activity on the spontaenous EEG increased to 66.5±17.5 µV on the 4th day of ANOH (versus background of 55.8±14.9 µV) and held at this level up to the 96th day of ANOH (66.7±17.5 µV), after which it diminished to considerably below the background level (32.7±10.5 µV, $P<0.05$). The changes in amplitude of α-rhythm were less marked in the second group, but they retained the same tendency: the amplitude increased from 45.0±7.0 µV in the background to 60.0±14.0 µV only on the 16th day of ANOH, and after the 32d day it gradually decreased without reaching background levels, even on the 176th day (46.8±7.4 µV). In the first group, there was unreliable change in amplitude of α-rhythm during ANOH.

There was gradual decrease in dominant activity on the spontaneous EEG during ANOH, and it was the most significant in the first (from 10.2±0.3 Hz in the background to 8.9±0.8 Hz on the 176th day of ANOH, $P<0.05$) and second (from 10.1±0.2 to 9.3±0.3 Hz, $P<0.05$) groups. The α-rhythm index dropped (from 30.8±8.8 to 16.6±8.8%, $P<0.05$, in the first group; from 55.0±11.4 to 30.0±7.0%, $P<0.05$, in the second and from 61.6±14.0 to 32.5±10.5%, $P<0.05$, in the third).

Visual analysis of the spontaneous EEG revealed that diffuse β-activity was the most marked at the start (4th and 16th days) and end (176th day) of ANOH. In addition, there were segments of low-frequency (14-25 Hz), high-amplitude β-rhythm throughout the ANOH period. On the 176th day of ANOH, the amplitude of β-activity increased to 36.6±7.8 µV in the third group, 32.3±4.7 µV in the second and 22.6±1.8 µV in the first ($P<0.05$).

Regional differences, which were the most marked in the third group, were noted as a result of decrease (and often disappearance at the end of ANOH) in α-activity of the anterocentral parts of the brain. The index of zonal differences on the 176th day of ANOH rose to 4.9±1.2 in the third group, 3.5±1.2 in the second and 3.0±0.7 in the first.

Slow-wave amplitude increased during ANOH, while frequency diminished the most in the third group. The amplitude of slow activity on the 176th day of ANOH increased to 45.0±7.0 μV ($P<0.05$) in the third group, 33.5±4.7 μV ($P<0.05$) in the second and 30.8±2.6 μV ($P>0.05$) in the first. The frequency of slow activity in the third group began to decline as early as the 16th day of ANOH (5.3±0.3 Hz) and constituted 4.5±0.3 Hz ($P<0.05$) on the 128th day of ANOH. In the second group these changes were less marked: the frequency of slow activity began to decrease on the 32d day of ANOH (5.1±0.3 Hz) and constituted 4.5±0.2 Hz on the 176th day of ANOH ($P<0.05$). There was no change in frequency of slow activity in the first group throughout the period of ANOH.

The test with rhythmic photostimulation demonstrated intensification of the phasic reaction of bioelectric activity of the brain to flashes of light during ANOH. On the 4th day of ANOH there was an increase in number of responses with adoption of photostimulation rhythm at a frequency of 15-25 Hz and synchronization of α-activity at frequencies of 6-12 Hz. These changes were the most marked in the third group ($P<0.05$). In two subjects of the first group who presented changes in background rhythm during photostimulation at a frequency of 15 Hz we observed appearance of sharp waves (in P-v, 36 years of age, on the 4th day of ANOH) and bilaterally synchronous paroxysmal discharges of 7/s with amplitude of up to 100 μV (in G-v, 37 years old, on the 16th day of ANOH).

During the second half of the ANOH period, there was a change in structure of bioelectric reactions of the brain to flashing light: upon stimulation at a frequency of 15-25 Hz the number of responses with adoption and change of rhythm diminished while the number of responses with depression and synchronization of activity increased. Conversely, at frequencies of 6-12 Hz, there was an increase in number of reactions with adoption and rechange in rhythm. Marked phasic changes in structure of bioelectric responses of the brain (in the frequency ranges of 15-25 and 6-12 Hz) were inherent in the second group ($P<0.05$).

The changes on the EEG during 3-min hyperventilation during ANOH presented the same direction as spontaneous bioelectric activity, and they were the most marked in the third group. There was appearance of paroxysmal, bilaterally synchronous slow activity (5-6 Hz, up to 200 μV) during hyperventilation in 5 subjects (1 in the second group, 2 in the first and 2 in the third), in all cases associated with changes in the background EEG. In these subjects, paroxysmal activity was recorded on the 4th day of ANOH, 4th and 15th days of the recovery period, less often on the 16th and 176th days of ANOH, 30th and 50th days of the rehabilitation period, and it was marked primarily in the central regions of the cerebral cortex. In 3 subjects with changes in the background EEG (1 from each group), there was appearance of locally impaired type of bioelectric brain activity with unilateral demonstration of a focus of slow activity (up to 70 μV) on the 61st, 96th, 128th and 176th days of ANOH, as well as in the rehabilitation period at the height of hyperventilation, while hyperventilation was associated at the above times with motor restlessness and complaints of headache, dry mouth, sensation of numbness in the arms and legs.

There was a significant difference between bioelectric activity of the brain in the recovery period and the background. The amplitude, frequency and index of α-activity on the spontaneous EEG were below background levels ($P<0.05$) throughout all 50 days of the recovery period, while the index of zonal differences, amplitude of β- and slow activity were above base levels ($P<0.05$). These changes were the most marked in the third group and the least marked in the first. Throughout the entire recovery period, the number of responses with rhythm adoption to rhythmic photostimulation at a frequency of 15-25 Hz was greater than in the background ($P<0.05$), with synchronization of α-activity in the range of 6-12 Hz. In 3 subjects with changes in the background EEG, we observed bilaterally synchronous paroxysmal activity, manifested mainly in the central zones of the cerebral cortex, up to the 50th day of rehabilitation during hyperventilation. The localized nature of the EEG persisted on the 50th day of the recovery period in 1 subject (second group).

As can be seen from the above findings, prolonged ANOH led to intensification of mild pathological signs observed in some subjects prior to the study. Considering the different degree of background changes in bioelectric activity of the brain (the least in the third group and the greatest in the first) and the submitted results, it can be concluded that the greatest changes in bioelectric activity of the brain during ANOH were noted in the third group and the least in the first.

The results of the studies during the recovery period revealed that the EEG was closest to the background in the first group and farthest in the third. The incomplete recovery of EEG parameters indicates the severity of changes in bioelectric activity of the brain observed during ANOH, on the one hand, and the prolonged period of recovery, in spite of the set of therapeutic and rehabilitation measures used, on the other.

We can assess the functional state and capabilities of the central nervous system to some extent on the basis of the distinctive changes in main parameters of bioelectric activity of the brain [5-10].

Increased activation of the cerebral cortex is reflected on the EEG by an increase in β-activity and occasionally appearance of sharp waves and spikes[5, 7, 9-12]. During rhythmic photostimulation, the range of adopted rhythms shifts in the direction of higher frequencies, while in the range of low ones there is an increase in respones with synchronization of α-activity [7, 11, 13, 15].

As shown by the results of this study, there was an increase in number and amplitude of β-waves on the 4th, 16th and 176th days of ANOH and in the recovery period; upon photostimulation, some of the subjects presented sharp waves and bilaterally synchronous paroxysms of θ-rhythm, as well as change in structure of bioelectric responses of the brain to flashing light: greater adoption of rhythm and change therein in the range of high frequencies, as well as synchronization of α-rhythm in the low-frequency range. The presence of these changes in spontaneous bioelectric activity of the brain during functional loads at the above stages of hypokinesia and absence thereof in the middle and at the end of the ANOH period apparently indicates an increase in excitability of the central nervous system at these times, not only with reference to the cerebral cortex, but mesodiencephalic structures.

The heightened excitability of the central nervous system, as demonstrated by the REG and EEG dynamics in the second and third groups of subjects, during the first week of ANOH was apparently attributable to early change in regulatory mechanisms of supplying blood to the brain under the unusual ANOH conditions [16]. On the first day of the recovery period, it was apparently induced by development of reactive hyperemia of the brain in response to ischemia during the last weeks of ANOH and general reaction to termination thereof [17-21].

The phasic changes we observed in bioelectric activity of the brain during ANOH were analogous to those previously described [19, 21].

Studies of the use of pharmacological agents [9, 22], internal and supraliminal inhibition [5, 11, 13, 23, 24], diffuse sleep [6, 7, 12, 14, 25, 26] and narcotic [27] inhibition revealed that prevalence of inhibitory processes in the central nervous system is reflected on the EEG by slowing of main rhythms, decreased amplitude of electric oscillations, increased diffuse, polymorphic, slow activity, as well as decrease in its frequency.

It was previously demonstrated that during sleep the reaction of repeating the rhythm of light flashes had a lower frequency than when awake [25]. In the presence of deeper anesthesia, the evoked reactions to rhythmic stimulation are much less marked than in the background tests [27]. In other words, there is prevalence of low-frequency changes in rhythm when there is a low level of cortical activation in response to flashing light, whereas in the range of high frequencies there is either minimal or no adoption of rhythm [13, 28].

Consequently, analogous EEG changes during the second half of the ANOH period can apparently be attributed to prevalence of inhibitory states in the central nervous system related to increased general asthenization of the body [17, 18]. The latter, as well as impairment of cortical-subcortical correlations, with prevalence of inhibitory processes in the cortex, probably explains the rapid fatigability of the subjects during the functional tests, their drowsiness at the end of the ANOH period, as well as appearance of locally impaired EEG in some of the subjects, with a unilateral focus of high-amplitude polymorphic δ-activity. As we know, there is prevalence of high-amplitude slow oscillations of potential in the presence of diffuse sleep inhibition [6, 7, 25].

Appearance of locally impaired bioelectric activity of the brain could also result from cerebral circulatory disorders. This possibility is indicated by the data of Kh. Kh. Yarullin et al. [29], who observed that there was an increase in phasic changes and appearance of asymmetry of rheoencephalographic parameters of pulsed circulation and vascular tonus with increase in duration of hypokinesia.

The obtained data indicate that the dynamics of the spontaneous EEG (amplitude, frequency, rhythms), as well as changes therein in response to flashing light and hyperventilation, are important indices for evaluation of the functional state of the brain and, particularly, diminished cortical activity.

BIBLIOGRAPHY

1. Kakurin, L. I.; Katkovskiy, B. S.; Tishler, V. A.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1978, pp 20-27.

2. Voskresenskiy, A. D.; Yegorov, B. B.; Pestov, I. D.; et al. Ibid, No 4, 1972, pp 28-32.

3. Zhirmunskaya, Ye. A. "Electric Activity of the Brain Under Normal Conditions, in the Presence of Essential Hypertension and Cerebrovascular Accident," Moscow, 1963, p 38.

4. Gubler, Ye. V., and Genkin, A. A. "Use of Nonparametric Statistical Criteria in Biomedical Research," Leningrad, 1973.

5. Anokhin, P. K. "Biology and Neurophysiology of Conditioned Reflexes," Moscow, 1968.

6. Latash, L. P. "The Hypothalamus, Adaptive Activity and Electroencephalogram," Moscow, 1968.

7. Novikova, L. A., and Farber, D. A. in "Vozrastnaya fiziologiya" [Age-Related Physiology], Leningrad, 1975, pp 491-622.

8. Povorinskiy, A. G. in "Kliniko-elektrofiziologicheskiye pokazateli funktsional'nogo sostoyaniya golovnogo mozga cheloveka" [Clinical and Electrophysiological Parameters of the Functional State of the Human Brain], Leningrad, 1971, pp 68-109.

9. Rusinov, V. S. in "Fiziologiya vysshey nervnoy deyatel'nosti" [Physiology of Higher Nervous Activity], Moscow, Pt 1, 1970, pp 356-429.

10. Spilker, B.; Kamiya, J.; Callaway, E.; et al. PSYCHOPHYSIOLOGY, Vol 5, 1969, pp 683-695.

11. Livanov, M. N., and Knipst, I. N. in "Fiziologiya vysshey nervnoy deyatel'nosti," Moscow, Pt 1, 1970, pp 294-355.

12. Dement, W. C. in "Comprehensive Textbook of Psychiatry," A. M. Freedman and H. I. Kaplan (editors), Baltimore, 1967, pp 77-88.

13. Gusel'nikov, V. I. "Electrophysiology of the Brain," Moscow, 1976.

14. Zhirmunskaya, Ye. A. in "Klinicheskaya neyrofiziologiya" [Clinical Neurophysiology], Leningrad, 1972, pp 224-265.

15. Kammel', Kh. R. KOSMICHESKAYA BIOL., No 1, 1973, pp 75-81.

16. Ingvar, D. H.; Sjolund, B.; and Ardo, A. ELECTROENCEPH. CLIN. NEUROPHYSIOL., Vol 41, 1976, pp 268-276.

17. Krupina, T. N., and Tizul, A. Ya. KOSMICHESKAYA BIOL., No 6, 1977, pp 26-31.

18. Panov, A. G.; Lobzin, V. S.; and Mikhaylenko, A. A. in "Sistema adaptatsii cheloveka i vneshnyaya sreda" [The System of Human Adaptation and the Environment], Leningrad, 1975, pp 124-132.

19. Petukhov, B. N., and Purakhin, Yu. N. KOSMICHESKAYA BIOL., No 5, 1968, pp 56-61.

20. Serapetinides, E. A.; Shurley, J. T.; Brooks, R.; et al. AEROSPACE MED., Vol 42, 1971, pp 840-842.

21. Pokrovskaya, Z. A.; Rossinskiy, O. G.; and Shaposhnikov, Ye. A. FIZIOLOGIYA CHELOVEKA [Human Physiology], No 2, 1976, pp 318-324.

22. Il'yuchenok, R. Yu. in "Fiziologiya vysshey nervnoy deyatel'nosti," Moscow, Pt 2, 1971, pp 256-289.

23. Asratyan, E. A. Ibid, Pt 1, 1970, pp 75-134.

24. Kopell, B. C.; Wittner, W. K.; Lunde, D.; et al. PSYCHOSOM. MED., Vol 32, 1970, pp 39-49.

25. Shapoval'nikov, A. N. in "Fiziologiya vysshey nervnoy deyatel'nosti," Moscow, Pt 2, 1971, pp 128-163.

26. Winters, W. D. ELECTROENCEPH. CLIN. NEUROPHYSIOL., Vol 17, 1964, pp 234-245.

27. Mikhaylovich, V. A. in "Klinicheskaya neyrofiziologiya," Leningrad, 1972, pp 474-493.

28. Lebedeva, L. I. in "Metody klinicheskoy neyrofiziologii" [Methods of Clinical Neurophysiology], Leningrad, 1977, pp 40-66.

29. Yarullin, Kh. Kh.; Krupina, T. N.; Vasil'yeva, T. D.; et al. KOSMICHESKAYA BIOL., No 4, 1972, pp 33-39.

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MORPHOMETRIC ANALYSIS OF GLOMERULES AND JUXTAGLOMERULAR SYSTEM OF THE RAT KIDNEY IN THE COURSE OF EXPERIMENTAL HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by I. P. Chernov and A. G. Gaffarov, submitted 30 Jan 78]

[English abstract from source]

In the hypokinetic study a certain correlation between variations in the means of the volume of cortical and juxtamedullary glomerules and the function of the juxtaglomerular apparatus has been established. It is hypothesized that at early hypokinesia renal vascular changes are nonspecific. The phenomenon of renal excretion of fluids and electrolytes is explained in terms of a simultaneous increase in the renin-angiotensin activity and 11-hydroxycorticosteroid content in plasma.

[Text] Importance is attributed to impairment of fluid-electrolyte metabolism in the pathogenesis of the hypokinetic syndrome [1-3]. These disturbances are based on changes in regulatory influence of the nervous and humoral systems on the kidney, general and renal hemodynamics [4-7]. It is quite obvious that we could not understand completely the nature and severity of changes in renal function without studying the structural changes associated with them.

We have tried to analyze here the state of renal vessels under hypokinetic conditions by means of histological and morphometric methods, and to compare the demonstrated changes to activity of cells of the juxtaglomerular system (JGS), which is directly involved in regulation of hemodynamics, transport of fluid and electrolytes.

Methods

We conducted this study on 70 male mongrel rats with an initial weight of 150-170 g. We created hypokinesia by keeping the animals in box-cages. The animals were decapitated after 3 h, and on the 1st, 3d, 5th, 10th, 20th and 30th days of the experiment. An ocular micrometer was used to measure the short (B) and long (L) diameters of cortical and juxtamedullary glomerules on kidney sections from experimental and control rats. We differentiated between these glomerules according to their topographic location [8] and size of afferent and efferent vessels [9]. We counted up 50 cortical and 50 juxtamedullary glomerules on several sections referable to 6 animals at each examination. The volume (in cubic micrometers) was calculated with the following formula:

$$V = \frac{\pi}{6} (LB)^{3/2}$$

To obtain a more graphic expression of the effect of hypokinesia, the absolute mean volume was expressed as a percentage of the control, taken as 100%. We assessed the JGS by determining granularity of its cells stained according to Bowie and then calculating the juxtaglomerular index (JGI). On the basis of the data in the literature [10], we made a distinction between four grades of granularity. The calculation was made with the following formula:

$$JGI = \frac{1n_1 + 2n_2 + 4n_3 + 8n_4}{N},$$

where n_1, n_2, n_3 and n_4 refer to the number of JGS cells with each grade of granularity, N is the total number of glomerules in the preparation [11]. Fluorimetry was used [12] to determine 11-HOC [hydroxycorticosteroids] in blood plasma at different stages of hypokinesia. The results were submitted to processing by the method of variational statistics [13]. Reliability was determined with the criterion of Student.

Results and Discussion

At the early stages of hypokinesia (3 h and 1 day) there were morphological signs of redistribution of blood in the kidney. They consisted of spasm of small arteries and arterioles of the cortex, considerable dilatation and plethora of arcuate veins and straight vessels of the medullary layer. There was a statistically significant decrease in volume of subcapillary glomerules and those of the external cortical layers, while those of the juxtamedullary zone were reliable greater in volume than the control level (see Table). By the 3d experimental day, both the medullary layer and cortex were plethoric, and not only vascular glomerules of renal corpuscles, but the capillary system of the tubules were subject to marked dilatation. The medullary vessels remained dilated. On the 5th day of hypokinesia, the capillaries of the juxtamedullary glomerules were still plethoric, whereas there was prevalence of glomerules with collapsed capillaries in the cortex. Thereafter (10th, 20th, 30th days) there was a tendency toward decreased plethora of capillaries, as well as cortical and juxtamedullary glomerules.

At the first two examinations, the morphological changes in JGS of the kidneys were characterized by an increase in number of cells corresponding to grades 3-4 granularity, while the JGI presented a statistically significant rise. It constituted 36.4±1.7 days after 3 h and 35.6±1.1 after 1 day (versus 28.1±1.2 in control rats). JGI did not differ appreciably from control levels on the 3d day of hypokinesia. On the 5th experimental day, we observed a maximum elevation of JGI (to 38.8±0.7). It declined thereafter. By the 10th day of hypokinesia JGI was negligibly above the control level, whereas on the 20th and 30th days we observed a decrease in both number of myoepithelioid cells, and in degree of granularity. The JGI dropped to 16.2±1.6 on the 20th day and to 22.3±0.9 on the 30th day.

Mean volumes of cortical and juxtamedullary glomerules of rat kidneys under hypokinetic conditions (n = 6)

Time	Glomerules					
	cortical			juxtamedullary		
	volume		P	volume		P
	thousands of μm^3	% of control		thousands of μm^3	% of control	
Intact rats	176,6±1,035	100.0±0,59		198,8±1,034	100,0±0,52	
After 3 h	169,5±1,077	96,0±0.61	0,001	220,3±0,934	110,8±0,47	0,001
1st day	158,4±1,148	89,7±0,65	0,001	206,2±0.994	103,7±0,50	0,001
3d "	203,6±0,90	115,3±0,51	0,001	242,9±0,855	122,2±0,43	0,001
5th "	145,2±1,254	82,2±0,71	0,001	206,6±0,994	103,9±0,50	0,001
10th "	169,0±1,077	95,7±0,61	0,001	181,7±1,133	91,4±0,57	0,001
20th "	158,4±1,148	89,7±0,65	0,001	194,4±1,054	97,8±0,53	0,02
30th "	156,3±1,166	88,5±0,66	0,001	172,8± 1,193	86,9±0.60	0.001

Note: P refers to reliability of difference between experimental and control rats, with regard to glomerular volume.

It is apparent from the foregoing that there is a certain correlation between volume of cortical and juxtamedullary glomerules, on the one hand, and activity of JGS cells, on the other. The increase in functional activity of the JGS occurred during periods of redistribution of intrarenal blood flow, when there was morphological demonstration of cortical ischemia and plethora of juxtamedullary glomerules and cortical vessels. As we know, the phenomenon of shunting of renal blood occurs with various extreme factors and states [9, 14, 15], and it is one of the "defense reaction" effects [16].

It was established that cortical vasoconstriction is related not only to extrarenal mechanisms, but is also considered as one of the variants of autoregulation of renal blood flow, where the JGS occupies a special place [17]. The redistribution of intrarenal circulation between the cortical and juxtamedullary nephrons, which differ in capacity to reabsorb sodium [18], which occurs under hypokinetic conditions, may be one of the causes of the change in excretory function of the kidneys.

The decline of the JGI on the 20th and 30th days of hypokinesia corresponded in our experiments to a decrease in filling of cortical and juxtamedullary glomerules. It is difficult to determine the cause-and-effect correlation between these changes, since the question of localization of the vascular effect of renin in the kidneys has still not been answered. Moreover, the decline of JGI could occur due to decreased synthesis of renin or degranulation of myoepithelioid cells as a result of increased excretion thereof in blood plasma.

Activation of the renin-angiotensin system, which was observed at the early stages of the experiment, is consistent with the findings of other authors [19], and it was demonstrable during the period of increased functional activity of the adrenals. 11-HOC content of blood plasma increased to 14.83 μg% on the 3d day, versus 6.3 μg% in intact rats. Hyperadrenocorticism persisted on the 10th and 20th experimental days, although the mean 11-HOC levels at these times were lower (9.8±0.001 and 8.8±0.004 μg%, respectively).

It was shown that the nature of renal exretory function in response to administration of angiotensin depends on a number of conditions, including the animal species, its "steroid status," direction of related changes in glomerular filtration and renal blood flow [20]. It was previously reported [21] that administration of renin and angiotensin induces natriuresis and diuresis in rats (unlike man). This occurs as a reuslt of increase in the filtration fraction, decreased tubular reabsorption of sodium, attenuation of passive and active processes of reabsorption of fluid in the distal tubules. Depending on the secretion level, corticosteroids have a different influence on the effect of angiotensin. In the presence of states involving excessive corticosteroids there is enhancement of the effect of angiotensin [20]. Experiments involving administration of ACTH and hydrocortisone to rats demonstrated that this is associated with elevation of the renin substrate. In addition, adrenocortical hormones enhance pressor sensitivity to renin and angiotensin, which occurs as a result of a change in fluid-sodium balance and electrolyte composition of the vascular wall. The diuretic and natriuretic effects of glucocorticodes are also attributed to their antialdosterone effect in and outside the kidney, influence on renal hemodyanmics and the blocking of the ADH [antidiuretic hormone] effect [22]. The regulatory role of glucocorticoids in tubular permeability to fluids was demonstrated in experiments involving microperfusion of the tubules of healthy and adrenalectomized rats given glucocorticoids and mineralocorticoids [23]. In adrenalectomized rats, permeability of the wall of the distal tubules to fluid increased, and it reverted to normal only after giving them glucocorticoids. Thus, the submitted data show that the increases elimination of fluid and electrolytes observed in hypokinetic rats [3, 7] is due to activation of the renin-angiotensin system, the effect of whose hormones is apparently simulated by glucocorticoides. The latter circumstance, by virtue of antialdosterone effect and direct effect on filtration and tubular reabsorption, has a substantial influence on fluid-electrolyte metabolism under hypokinetic conditions.

BIBLIOGRAPHY

1. Kozyrevskaya, G. I. "Effect of Experimental Restriction of Muscular Activity and Space Flight Conditions on Fluid-Electrolyte Metabolism in Man," candidatorial dissertation, Moscow, 1970.

2. Grigor'yev, A. I. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 6, 1972, pp 828-835.

3. Kovalenko, Ye. A., et al. USPEKHI FIZIOL. NAUK [Advances in Physiological Sciences], Vol 6, No 3, 1975, pp 110-136.

4. Mogendovich, M. R., and Ryklin, M. G. in "Fiziologiya i patologiya motorno-vistseral'nykh refleksov" [Physiology and Pathology of Visceromotor Reflexes], Perm', 1961, pp 49-60.

5. Andrianova, L. A. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1971, pp 26-29.

6. Shkhvatsabaya, I. K., et al. in "Kosmicheskaya biologiya i aviakosmicheskaya meditsina" [Space Biology and Aerospace Medicine], Moscow--Kaluga, Vol 1, 1972, pp 97-99.

7. Osipov, Yu. Yu., and Shashkov, V. S. KOSMICHESKAYA BIOL., No 1, 1973, pp 17-21.

8. Natochin, Yu. V. "Ion Regulating Renal Function," Leningrad, 1976.

9. Serov, V. V. "Morphological Bases of Renal Immunopathology," Moscow, 1968.

10. Hartroft, P. M., and Hartroft, W. S. J. EXP. MED., Vol 97, 1953, pp 415-420.

11. Vikhert, A. M.; Serebrovskaya, Yu. A.; and Tinyakov, Yu. G. ARKH. PAT. [Archives of Pathology], No 2, 1963, pp 17-24.

12. Usvatova, I. Ya., and Pankov, Yu. A. in "Sovremennyye metody opredeleniya steroidnykh gormonov v biologicheskikh zhidkostyakh" [Modern Methods for Assaying Steroid Hormones in Biological Fluids], Moscow, 1968, pp 38-48.

13. Avtandilov, G. G. "Morphometry in Pathology," Moscow, 1973.

14. Braun, M. D., and Leykin, M. D. ARKH. PAT., No 11, 1972, pp 51-56.

15. Pankova, A. S., and Savina, Ye. A. KOSMICHESKAYA BIOL., No 3, 1973, pp 8-12.

16. Pytel', A. Ya., and Goligorskiy, S. D. "Acute Renal Insufficiency," Kishinev, 1963.

17. Kovalevskiy, G. V. ARKH. PAT., No 2, 1963, pp 24-33.

18. Merzon, A. K. in "Fiziologiya pochki" [Physiology of the Kidney], Leningrad, 1972, pp 41-82.

19. Polyak, M. G.; Sokolova, G. P.; and Shorin, Yu. P. in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinesii" [Adaptation to Muscular Activity and Hypokinesia], Novosibirsk, 1970, pp 139-141.

20. Serebrovskaya, Yu. A. PAT. FISIOL. [Pathological Physiology], No 3, 1964, pp 87-92.

21. Vikhert, A. M., and Uskalov, A. F. KARDIOLOGIYA [Cardiology], No 3, 1971, pp 143-156.

22. Bondarenko, B. B. in "Fiziologiya pochki," Leningrad, 1972, pp 221-235.

23. Stolte, H.; Brecht, J. R.; Widerholt, M.; et al. PFLUG. ARCH. GES. PHYSIOL., Vol 299, 1968, pp 99-102.

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EFFECT OF HYPOKINESIA ON CHANGES IN CARBOHYDRATE AND LIPID METABOLISM IN THE HEART AND LIVER

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[English abstract from source]

Rigid immobilization of rabbits is accompanied by a reduction of glycolysis rate in the liver and, particularly, in the heart, and a simultaneous increase of the fraction of carbohydrate utilization in the pentose phosphate pathway. It is also followed by cholesterol accumulation in the blood and tissues in spite of an accelerated bile excretion of cholesterol and its derivatives — bile acids.

[Text] Inadequate physical activity increases the possibility of atherosclerosis and raises by 1.5-2 times the probability of myocardial infarction [1-3]. Experimental restriction of muscular activity is associated with changes in metabolic processes that are similar in nature to the changes observed with atherosclerosis [4-6]. The cholesterol and β-lipoprotein content of blood serum increases, and in tissues there is an increase in cholesterol with concurrent decrease in total lipids.

We have studied here the rate of assimilation of carbohydrates via glycolysis and the pentose-phosphate pathway, as well as changes in B bile in hypokinetic rabbits.

Methods

Experiments were conducted on 76 rabbits of both sexes weighing 2.5 to 3 kg. Control and experimental animals were kept on the usual feed diet. The experimental group of rabbits were kept in hypokinetic cages. We assayed glycogen [7], rate of glycolysis (according to difference between preformed lactate and increment thereof in 1 h of incubation in Krebs-Ringer buffer, pH 7.35 at 37°C with addition of 200 mg% glucose according to Barker and Summerson [8]) and activity of the pentose-phosphate pathway (according to level of preformed pentoses and sedoheptuloses, and decline or elevation thereof when incubated with glucose or fructose-1,6-diphosphate [9]) in the liver and heart of the animals on the 10th, 15th, 30th and 60th experimental days. On the same days, we assayed B bile, cholesterol (according to Sperry and Brady as modified by P. Z. Khasigov [10]), bile acids (according to Shire-Kuhne as modified by N. P. Skakun [11]) and dry residue.

Results and Discussion

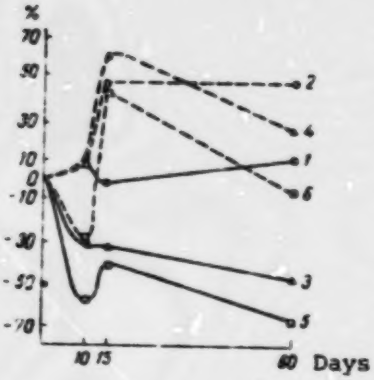
There was an appreciable decrease in liver glycogen content as a result of hypokinesia (by 64.12, 75.24, 81.68 and 82.83% after 10, 15, 30 and 60 days). Conversely, there was a reliable increase in glycogen content of the heart at the start of the experiment, followed by gradual decrease. By the 60th day, glycogen level in the heart was one-half the control level.

There was a tendency toward decrease in preformed lactate in the heart and liver (Table 1). Upon incubation of homogenates of these organs with glucose, lactate increment by the 10th day of hypokinesia was one-half the control level in the heart and remained at this level to the end of the study; in the liver it remained low to the 15th day.

Table 1. Changes in rate of glycolysis in tissues of hypokinetic rabbits

Duration of experiment, days	Number of animals	Statistical index	Lactate content, μmole/100 mg wet tissue			
			liver		heart	
			preformed	increment with incub. with glucose	preformed	increment with incub. with glucose
Control	7	M±m	0,82±0,05	0,79±0,02	2,64±0,06	2,16±0,04
10	6	M±m	0,54±0,12	0,40±0,04	2,16±0,34	1,03±0,41
		%	—34,15	—49,37	—18,18	—52,31
		P	>0,05	<0.01	>0.1	<0,02
15	5	M±m	0,55±0,04	0,52±0,06	2,52±0,18	1,50±0,18
		%	—32,93	—34,18	—4,55	—30,56
		P	<0,01	<0,01	>0,5	<0.01
30	5	M±m	0,62±0,08	0,71±0,10	1,86±0.14	0,78±0,17
		%	—24,39	—10,13	—29,55	—63,89
		P	>0,05	>0,4	<0,01	<0,01
60	5	M±m	0,70±0,08	0,66±0.15	2,80±0,20	1,15±0,12
		%	—14,63	—16,46	+6,06	—46,76
		P	>0,1	>0,4	>0,4	<0,01

There was a greater decrease in pentose content upon incubation of homogenates of the heart with glucose, as compared to the control (by 31.71, 32.78 and 49.05% after 10, 15 and 60 days, respectively), increase in sedoheptuloses (by 57.77% after 15 days and 23.19% after 60 days), with preservation of a constant level of preformed pentoses and sedoheptuloses



Levels of preformed pentoses (1) and sedoheptuloses (2) in heart tissue and changes therein upon incubation with glucose (3 and 4, respectively) and fructose-1,6-diphosphate (5 and 6) under hypokinetic conditions

(see Figure). When heart tissues were incubated with fructose-1,6-diphosphate, there was a more significant decrease in pentose content (by 57.17, 43.22 and 69.12% on the same days), but a reliable increase in sedoheptulose content (by 41.42%) was only noted after 2 weeks. Preformed pentose content of the liver remained constant. A tendency toward decrease therein was observed only by the end of the 2d experimental month (by 33.61%, $P>0.05$). When hepatic tissue was incubated with substrates the changes were also in the same direction: a tendency toward decrease in pentose content after 10 days (by 3.93%, as compared to glucose and by 13.13%, as compared to fructose-1,6-diphosphate), which was reliable by the end of the 2d week (by 13.24 and 15.20% respectively). However, by the end of the experiment, the decrease in pentose content upon incubation of homogenates with substrates did not differ from the control. While preformed sedoheptuloses maintained a constant level, by the end of the experiment the increment thereof in the liver upon incubation with both substrates was the most significant (by 73.70% with glucose and 53.79% with fructose-1,6-diphosphate).

Thus, under hypokinetic conditions there was a decrease in rate of oxidation of glucose by means of glycolysis, with concurrent increase in share of assimilation via the pentose-phosphate pathway.

There was structural change in composition of B bile under hypokinetic conditions (Table 2).

During the first month of the experiment, we observed an increase in B bile content, with maximum increment after 2 weeks of limited mobility. At the same time, there was an increase in concentration of cholesterol in bile (by 2.5 times between the 10th and 30th days, and 1.5 times at the end of the experiment) and mean of 2-fold increase in bile acids throughout the experiment. There was also a reliable increase in amount of dry residue in the bile, as compared to the control.

Glycogen content of hepatic tissue diminished, apparently due to hyperproduction of catecholamines, the levels of which were significantly elevated in blood and urine at different stages of hypokinesia [6, 12-14]. The decrease in rate of glycolysis in liver and heart tissues is possibly due to excessive accumulation of cholesterol in blood and tissues in the presence of hypokinesia [4-6, 15-18]. Excessive production of glucocorticoids under prolonged hypokinetic conditions [14] is also capable of depressing hexokinase activity [19].

Table 2. Changes in B bile parameters in hypokinetic rabbits

Duration of experiment, days	Statistical index	Bile, mℓ	Cholesterol mg%	Bile acids, mg%	Dry residue, %
Control	M±m	1,27±0,24	255,67±33,65	2311,09±209,71	13,90±1,04
	n	11	6	11	7
10	M±m	1,90±0,46	871,60±48,52	4712,40±104,87	20,49±1,91
	n	6	5	5	6
	%	+49,61	+240,91	+103,90	+47,41
	P	>0,2	<0,01	<0,01	<0,01
15	M±m	2,88±0,12	856,80±100,0	5557,20±853,31	21,05±2,05
	n	5	5	5	5
	%	+126,77	+235,12	+140,46	+51,44
	P	<0,01	<0,01	<0,01	<0,02
30	M±m	1,72±0,33	820,80±106,67	5664,80±800,54	23,37±2,49
	n	5	5	5	5
	%	+35,43	+221,04	+145,12	+68,13
	P	>0,2	<0,01	<0,01	<0,01
60	M±m	1,23±0,13	610,80±55,86	5102,00±733,47	20,62±0,57
	n	6	5	5	6
	%	—3,15	+138,90	+120,76	+48,34
	P	<0,9	<0,01	<0,01	<0,01

The increased assimilation of carbohydrates via the pentose-phosphate pathway, which is observed under hypokinetic conditions, could occur both as a result of decline of Michaelis constant for glucose-6-phosphate dehydrogenase and due to activation of this enzyme by catecholamines [20-22], while 6-phosphogluconate is also an inhibitor of glycolysis [23]. Activation of the pentose pathway with dissociation of respiration and phosphorylation, which can occur during hypokinesia as a result of hyperproduction of epinephrine [12-14, 23, 24], enables the body to come out of the critical state by means of increase in reserve of NADP·H_2 and ribose, which are needed for synthesis of lipids, nucleotides and nucleic acids. Activation of the pentose pathway in the heart makes it possible for cells of the contractile myocardium to recover as a result of mitochondrial hyperplasia [25].

The excessive production of epinephrine under hypokinetic conditions [12-14] causes changes in the myocardium [4, 26] and activation of lipolysis. However, the associated decrease in activity of citrate synthetase and acetoacetyl-CoA-thiolase [27], as well as inadequate oxygen uptake [15, 24], could cause accumulation in the body of products of incomplete oxidation of fatty acids [28]. The excessively accumulated acetone bodies are apparently not only eliminated, but utilized for synthesis of cholesterol and fatty acids, which is added by replenishment in tissues of $NADP \cdot H_2$ reserves as a result of activation of the pentose pathway. There is progressive increase in blood and tissular β-lipoprotein content with increase in duration of hypokinesia [4-6, 15, 16], which indirectly favors the above hypothesis. The elevation of levels of 6-phosphogluconate and transport forms of cholesterol decreases the activity of enzymes of the glycolytic pathway, closing the circle of changes in metabolic processes in the presence of "rigid" hypokinesia.

In an effort to get rid of excessive cholesterol, the body eliminates it in bile and there is more active transformation into bile acids (see Table 2). Activation of this process conforms with maximum increase in blood cholesterol [6, 15, 16], and it is observed 2-3 weeks after the start of hypokinesia. The progressive hyper-β-lipoproteinemia associated with restricted movement is the factor that stimulates bile production, since synthesis of bile acids is possible only at the expense of β-lipoprotein cholesterol [29]. The increased transformation of cholesterol into bile acids, as well as intensified elimination thereof in bile, are adaptive reactions of the body that permit it to partially rid itself of excessive amounts thereof. On the first days of restricted movement, part of the cholesterol is apparently converted into corticosteroids, since the levels thereof in blood increase [5]. However, synthesis of corticosteroids and sex hormones from cholesterol can only occur when there is adequate activity of the tricarboxylic acid cycle, since oxidation of the side chain of cholesterol for production of progesterone requires adequate amounts of pyruvate, malate and NADP [30]. In the case of prolonged hypokinesia, utilization of cholesterol for synthesis of sex hormones and corticosteroids apparently diminishes, due to decreased activity of Krebs' cycle [27].

When there was inadequate physical activity, there was an increase in cholesterol content of the heart and, particularly, the liver, which was more significant in old animals, in spite of the above-mentioned defense mechanisms [6, 15]. We were impressed by the close correlation between levels of cholesterol in blood, tissues and bile (see Figure). The decreased elimination of cholesterol in bile toward the end of the 2d month of hypokinesia was associated with concurrent elevation of its level in blood and the liver.

Consequently, under hypokinetic conditions the fatty acids from the pool, as well as those synthesized de novo, undergoing partial oxidation, replenish the reserve of acetone bodies, which are either eliminated from the body or utilized again for synthesis of fatty acids and cholesterol. Cholesterol is metabolically less active, and for this reason the level thereof gradually rises in blood and tissues under hypokinetic conditions.

BIBLIOGRAPHY

1. Morris, J. N., and Crawford, M. D. BRIT. MED. J., Vol 2, 1958, pp 1485-1496.

2. Breslow, L., and Bull, P. J. CHRON. DIS., Vol 11, 1960, pp 421-444.

3. Acheson, R. M. YALE J. BIOL. MED., Vol 35, 1962, pp 143-170.

4. Tyavokin, V. V. "Hypodynamia and Cardiovascular Pathology," Saransk, 1975.

5. Parin, V. V.; Krupina, T. N.; Mikhaylovskiy, G. P.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1970, pp 59-64.

6. Fedorov, I. V.; Ryl'nikov, Yu. P.; and Lobova, T. M. KARDIOLOGIYA [Cardiology], No 7, 1973, pp 50-54.

7. Kemp, A., and Kits, J. M. BIOCHEM. J., Vol 56, 1954, pp 646-648.

8. Barker, S. B., and Summerson, W. H. J. BIOL. CHEM., Vol 138, 1941, pp 535-543.

9. Golovatskiy, I. D. UKR. BIOKHIM. ZH. [Ukrainian Biochemical Journal], No 6, 1965, pp 933-934.

10. Khasigov, P. Z. "Effect of Choline on Cholesterol Metabolism in Fasting Rabbits," candidatorial dissertation, Leningrad, 1959.

11. Skakun, N. P. "Fundamentals of Pharmacology of the Bile-Secreting Process," doctoral dissertation, L'vov--Ternopol', 1959.

12. Kazaryan, V. A.; Pishchik, V. B.; and Shitov, G. D. in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii" [Adaptation to Muscular Activity and Hypokinesia], Novosibirsk, 1970, pp 79-80.

13. Novikova, L. A.: Savina, M. I.; Revich, G. G.; et al. in "Morfologicheskiye i fisiologicheskiye osnovy regulyatsii i vosstanovleniya funktsii organizma" [Morphological and Physiological Bases of Regulation and Restoration of Body Functions], Moscow, 1970, pp 85-87.

14. Tigranyan, R. A.; Belyakova, M. I.; Davidova, N. A.; et al. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, Vol 2, 1975, pp 187-190.

15. Ryl'nikov, Yu. P. KOSMICHESKAYA BIOL., No 2, 1974, pp 8-13.

16. Ryl'nikov, Yu. P., and Fedorov, I. V. in "Povolzhskaya konf. fiziologov s uchastiyem biokhimikov, farmakologov i morfologov. 6-ya. Materialy" [Proceedings of 6th Povolzh'ye Conference of Physiologists, With the Participation of Biochemists, Pharmacologists and Morphologists], Cheboksary, Vol 2, 1973, pp 126-126 [sic].

17. Il'in, V. S., and Titova, G. V. VOPR. MED. KHIMII [Problems of Medical Chemistry], No 4, 1956, pp 243-251.

18. Panin, L. Ye., and Polyakov, L. M. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 10, 1976, pp 1202-1204.

19. Shanygina, K. I. BIOKHIMIYA [Biochemistry], No 2, 1971, pp 363-366.

20. Maydanova, N. V. BYULL. EKSPER. BIOL., No 1, 1971, pp 67-69.

21. Maydanova, N. V., and Shevchuk, V. A. NAUCH. DOKL. VYSSH. SHKOLY. BIOL. NAUKI [Scientific Reports of Schools of Higher Education. Biological Sciences], No 3, 1976, pp 27-30.

22. Shanygina, K. I., and Novikova, N. A. VOPR. MED. KHIMII, No 3, 1977, pp 358-360.

23. Devlin, T. M.; Barnes, N. S.; and Pruss, M. P. BIOCHEM. BIOPHYS. RES. COMMUN., Vol 17, 1964, pp 443-448.

24. Kovalenko, Ye. A.; Popkov, V. L.; Kondrat'yev, Yu. I.; et al. PAT. FIZIOL. [Pathological Physiology], No 6, 1970, pp 3-9.

25. Paukov, V. S., and Khitrov, N. K. KARDIOLOGIYA, No 11, 1976, pp 24-31.

26. Kovalenko, Ye. A.; Mailyan, E. S.; Popkov, V. L.; et al. USPEKHI FIZIOL. NAUK [Advances in Physiological Sciences], Vol 6, No 3, 1975, pp 110-136.

27. Sharkova, Ye. V. in "Vsesoyuznyy biokhimicheskiy s"yezd. 3-y. Referaty nauch. soobshcheniy" [Abstracts of Scientific Papers Delivered at 3d All-Union Biochemical Congress], Riga, Vol 2, 1974, pp 339-339 [sic].

28. Lobova, T. M., and Chernyy, A. V. KOSMICHESKAYA BIOL., No 6, 1977, pp 36-40.

29. Sodchi, H. S., and Kudchodkar, B. J. LANCET, Vol 1, 1973, pp 513-519.

30. Boguslawski, W.; Klimek, J.; and Lelewski, L. ACTA BIOCHIM. POL., Vol 21, 1974, pp 119-124.

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EFFECT OF CONDITIONING FOR HYPOXIA ON FERTILITY OF WHITE MICE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by V. B. Malkin and Ye. A. Stroganova, submitted 7 Apr 78]

[English abstract from source]

The purpose of the study was to investigate a prolonged effect of hypoxia on the reproductive function and development of pups of white mice. Beginning with the age of 2 months the animals were exposed to an altitude of 5500 m for 6 hours a day during 9 months. The mice that were so adapted to and mated in hypoxia did not deliver any offspring. The animals that were adapted to hypoxia during intrauterine and postnatal development and mated at 5500 m delivered normal although much smaller litters.

[Text] Some researchers propose the use of an artificial gas environment with low partial oxygen pressure in the pressurized cabins of spacecraft to prevent asthenization of cosmonauts during long-term flights. This suggestion is based on the fact that adaptation to hypoxia has a stimulating effect on hemopoiesis, respiratory function and circulation.

A comparative evaluation of different conditioning regimens revealed that intermittent exposure to hypoxia (6-7 h/day) has a more marked conditioning effect than continuous exposure to the same altitude [1]. In view of the foregoing, there is reason to assume that with the use of an "active" hypoxic atmosphere one can select modes with which the cosmonauts would be exposed daily for several hours to the effects of insufficient oxygen in the inhaled air. This makes it necessary to pursue a comprehensive study of the effects of such conditioning not only on the functional state of the body, but such important biological parameters as reproductive capacity, mean life expectancy and others.

There is information in the literature to the effect that prolonged shortage of oxygen in inhaled air leads to depression of reproductive function [2, 3].

Experimental studies of the effects of hypoxia on animal fertility established that with increase in altitude to which the animals were exposed there was a decrease in fertility [1, 3, 4]. Evidently, both neuroendocrine changes in the female, as a result of which there is impairment of the mechanism of normal implantation of a fertilized ovum in the uterine wall [5], and the direct deleterious effect of hypoxia on the process of spermatogenesis, maturation of follicles and, perhaps, the embyro itself [6] are the causes of this decrease in fertility.

Our objective here was to study the effect of a prolonged shortage of oxygen in the gas environment on reproductive function of white mice and development of offspring.

Methods

Experiments were conducted on mongrel white mice at the age of 2 months. The study lasted 9 months. At the first stage of the experiment, all of the animals, with the exception of a control group, were adapted to hypoxia in a pressure chamber. Conditioning lasted 30 days, during which the animals were raised daily to increasing altitudes (from 3000 to 5500 m). They remained at each level for 6 h/day. Thereafter, to maintain the conditioning effect, the animals were divided into four groups. Each group consisted of 6-9 females and 3 males kept separately. The first group was exposed to an "altitude" of 5500 m for 6 h daily, with the exception of Sundays; the second was conditioned once a week ("altitude" of 5500 m for 6 h); the third was conditioned twice a week on the same schedule. The fourth group (control) was kept in the vivarium throughout the experiment. On the 56th day of the experiment, the males and females of all groups were put together for 15 days for mating, and conditioning on the same program continued in the pressure chamber. The animals were weighed before mating. In addition, we singled out a group of females that was put together with males for 5 h twice a week only at an "altitude" of 5500 m (altitude group). The general condition of animals in all groups was satisfactory after 2 months of the experiment, prior to mating. The mean weight of males constituted 25.5, 25, 27 and 31 g in the 1st, 2d, 3d and 4th groups, respectively; the mean weight of females constituted 23.6, 23.5, 26.3 and 25 g, respectively. In the altitude group, mean weight of males was 28 g and that of females was 26 g.

Results and Discussion

In the 1st-3d groups, whelping began at the same time, on the 21st-22d day. It started several days later in the 4th group, but occurred within 2 days, whereas in the first 3 groups it extended over 6-7 days.

In the 1st group, 3 out of 7 females dropped pups. The mean number of offpsring per female constituted 6.6. In the 2d group, 5 out of 7 females had offspring. There were 6.4 mice per female. In the 3d group, 8 out of 9 females gave birth. The mean number of offspring per female was 5.7. In the 4th group, 4 out of 6 females had offspring, with a mean of 5 mice per litter. Thus, whelping was at a lower level in the first group, which was submitted to the most intensive (daily) conditioning in the pressure chamber, than in the other groups.

Table 1. Reproductive capacity of mice in different groups and characteristics of their offspring

Index	Animal group							
	1		2		3		4	
	offspring (litter)							
	first	second	first	second	1st	2d	1st	2d
Whelping, day after putting male with female	22—29	23—24	22—28	21—25	21—27	21—30	25—26	24—26
Mean number of offspring per female	6,6	6,6	6,4	8,6	5,7	7,2	5	8
P	<0,01	<0,01	<0,01	>0,05	>0,05	>0,05	—	—
Mean weight of 1-day-old mice, g	—	1,4	—	1,3	—	1,7	—	1,5
P	—	>0,05	—	>0,05	—	>0,05	—	—
Mean wt. of 10-day-old mice, g	4,4	5,0	4,9	3,7	5,7	5,2	7,5	4,8
P	<0,01	>0,05	<0,01	>0,05	<0,01	>0,05	—	—
Mean wt. of 20-day-old mice, g	7,9	7,6	7,4	7,5	7,6	8,7	9,2	10,0
P	>0,05	<0,01	<0,01	<0,01	>0,05	>0,05	—	—
Mean wt. of 30-day-old mice, g	12,1	9,3	11,8	11,5	13,6	12,9	15,8	15,4
P	<0,05	<0,01	<0,01	<0,01	>0,05	>0,05	—	—

Note: Exposure to hypoxia before mating of the 1st, 2d and 3d groups lasted 55 days in obtaining the first litters of offspring and 138 days for the second litters.

As can be seen in Table 1, the mean number of mice per litter in the 1st and 2d groups was higher than in the 1st (control) group by 1.6 and 1.4, respectively. The results are statistically reliable (P<0.01). In the "altitude" group, only 1 out of 6 females had offspring on the 25th day. The litter consisted of one stillborn mouse. Thus, when males and females were mated only at an "altitude" of 5500 m there was a drastic decrease in reproduction (in fact, it was almost entirely suppressed). In the subsequent course of the experiment, we continued to condition the parents, together with the offspring, in the pressure chamber. We monitored development of the offspring from the time of birth. As shown in Table 1, the mice delivered by the 1st group of animals weighed an average of 2.7, 1.3 and 3.7 g less than in the control on the 10th, 20th and 30th days, respectively. These differences in weight were statistically reliable (P<0.005, P<0.01). The mean weight of offspring delivered by the second group of animals was 2.6, 1.8 and 4 g lower than in the control at the age of 10, 20 and 30 days, respectively. The results were statistically reliable (P<0.01). The mean weight of mice delivered by the 3d group was lower than in the control; however, these differences were statistically reliable only at the age of 10 days (P<0.01).

Fur growth began almost simultaneously in all groups. After 30 days, the offspring were separated from the parents and, like before, all of the animals (offspring and parents) continued to be conditioned to an "altitude" of 5500 m. At the age of 6.5 months, the parents were again put together for mating. Second litters were obtained in all groups. The mean weight of the offspring at birth was virtually the same in all 4 groups, ranging from 1.3 to 1.7 g. In the next 10 days, weight gain was uniform in offspring of the 1st, 3d and 4th groups. Only in the 2d group was there a tendency toward 1.4-g decrease in mean weight, as compared to the control. At the age of 20 days, the mean weight of mice in the 1st-3d groups was 2.4, 2.5 and 1.3 g less than in the control. The results were statistically reliable (P<0.01) in the 1st and 2d groups. At the age of 30 days, the mean weight of offspring in the 1st-3d groups was 6.1, 3.9 and 2.5 g less, respectively, than in the control. The difference was statistically reliable in the 1st group (P<0.01).

It was very interesting to see if offspring would be obtained from animals that had been exposed to hypoxia in the intrauterine period. For this purpose, we took mice from the first litters born to animals on the 76th-80th day of the experiment. At mating time these animals had reached the age of 4 months. By this time, the mean weight of males in the 1st-4th groups constituted 30, 30, 27 and 38 g, respectively, and that of females 22.8, 25.5, 25 and 35.3 g. In the "altitude" group, the mean weight of males was 30 g and females 35.3 g.

All groups of experimental animals produced offspring. Thus, it may be considered that animals preconditioned to hypoxia reproduced on virtually the normal (control) level. As can be seen in Table 2, in all three groups there were fewer mice per female that gave birth than in the 4th (control) group: by a mean of 1.9, 4.1 and 2.5, respectively. The differences were statistically reliable (P<0.01). In the "altitude" group, 2 out of 5 mice produced offspring. There was a mean of 5.5 mice per litter.

The mean weight of offspring at the age of 1 day was virtually the same in all groups. As shown in Table 2, weight gain for the next 10 days was uniform in all groups. However, at the age of 20 and 30 days, there was a lag in weight gain of animals in the 1st and 3d groups. Weight gain in animals born to the "altitude" group of parents was close to the control level. Interestingly enough, normal offspring was delivered by animals of the "altitude" group, which had been exposed to hypoxia from the time of birth, whereas no offspring had been obtained from their parents, i.e., animals first used in the experiment at the age of 2 months and put in the "altitude" group, in spite of the fact that these mice were of the same age. The increase in number of mice per second litter from parents weighing less can apparently be attributed to the fact that the females usually deliver considerably smaller offspring the first time. The offspring delivered by animals exposed to a shortage of oxygen in the pressure chamber during embryogenesis differed substantially in number from the control group. There were 1.9, 4.1 and 2.5 fewer mice per litter than in the control in the 1st-3d groups, respectively. The differences were statistically reliable. Reproduction was close to the control in females that were conditioned from the time of birth. Thus, reproductive capacity was somewhat higher in animals submitted to hypoxic conditioning while still in the intrauterine stage of development and periodically exposed from the time of birth to a gas environment markedly deficient in oxygen, i.e., animals adapted to the prolonged effect of hypoxia, than in mice exposed to hypoxia for the first time at the age of 2 months.

Table 2. Reproductive capacity of mice in different groups and characteristics of their offspring (third litters)

Index	Animal group				
	1	2	3	4	"altitude"
Exposure to hypoxia prior to mating, months	4	4	4		4
Day of whelping, from time male was put with female	20—23	20—28	20—23	20—26	19—25
Mean number of offspring per whelping female	7,2	5	6,6	9.1	5,5
P	<0,01	<0,01	<0,01	—	—
Mean wt. of day-old mouse, g	1,4	1,8	1,5	1,4	1,6
P	>0,05	>0,05	>0,05	—	—
Mean wt. of 10-day-old mouse, g	4,4	5,7	4,7	5,2	4,5
P	<0,05	>0,05	>0,05	—	—
Mean wt. of 20-day-old mouse, g	6,04	8,7	7.2	8	9
P	<0,01	>0,05	>0,05	—	—
Mean wt. of 30-day-old mouse, g	11,7	13,3	12,3	14,7	15,0
P	<0,01	>0,01	<0,01	—	—

As a result of this study, it was established that daily exposure of animals to oxygen-deficient conditions corresponding to an "altitude of 5500 m for 6 h/day did not prevent reproduction, unlike other conditioning programs.

Under the hypoxic conditioning schedule that we selected, the offspring developed normally, and there was only some lag in weight gain of newborn animals submitted to conditioning.

The above data and results of a previous study [1] are indicative of the desirability of using "split" programs of conditioning to hypoxia, i.e., a schedule that involves daily alternation of exposure to a shortage of oxygen and normal conditions.

BIBLIOGRAPHY

1. Malkin, V. B., and Gippenreyter, Ye. B. "Acute and Chronic Hypoxia," Moscow, 1977.

2. Arshavskiy, I. A. "Essays on Age-Related Physiology," Moscow, 1967.

3. Van Lear, E., and Stickney, K. "Hypoxia," Moscow, 1967.

4. Nelson, M. L.; Cons, J. M.; and Hodgdong, G. E. ENVIRONM. PHYSIOL. BIOCHEM., Vol 5, 1975, p 5.

5. Gordon, A. S.; Tornetta, F. J.; and Garipper, H. A. PROC. SOC. EXP. BIOL. (New York), Vol 53, 1943, p 6.

6. Altland, P. D., and Allen, E. J. MORPH., Vol 91, 1952, pp 541-553.

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THE QUESTION OF USING DEHYDRATED FOODS DURING LONG-TERM SPACE FLIGHTS

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[English abstract from source]

The paper discusses the results of five studies on 35 test subjects conducted to test diets of dehydrated products to be used in prolonged space flights. The studies have demonstrated that a diet consisting of only dehydrated food products can be used for a prolonged time (up to 1 year). Dehydrated foods after a 2-year storage and proton irradiation at a dose of 24,000 rad retain their biological value and assure an adequate nutritional status. On this basis a space diet composed of dehydrated foods has been developed.

[Text] Before reliable and economical methods are developed for producing food for long-term space flights, apparently the crew will consume primarily dehydrated products [1, 2].

Development of food rations consisting of dehydrated foodstuffs for long-term space flights requires determination of the possibility of long-term intake of dehydrated foods under ordinary living conditions and in a pressure chamber, as well as studies of the influence of storage time and possible levels and spectrum of radiation during long-term (up to 2 years) space flights on biological value of foods, determination of forms and assortment of dehydrated foods suitable to make up food rations for long-term space flights. We submit the results of these studies in this report.

Methods

We conducted 5 studies with the participation of 35 volunteer subjects ranging in age from 19 to 49 years. In the first study, 6 subjects were on a diet for 120 days consisting entirely of dehydrated foods, under customary living conditions. In the second study, 3 subjects received the same rations, but in a pressure chamber with an artificial habitat. For 1 month before and after the study, their diet consisted of freshly prepared foods analogous in chemical composition to the experimental ration. In the third and fourth series of studies, the dehydrated products had been stored for 2 years previously, and some were exposed to divided doses of proton radiation totaling 24,000 rad (6000 rad every 6 months). The radiation dose for the foods was determined on the basis of analysis of the radiation situation during long-term space flights over a period of several years, when the cumulative dose, referable chiefly to protons from solar bursts, could constitute tens of thousands of rad with shielding about 1 g/cm^2 in thickness [3]. The technique for irradiation was described previously [4]. In the third study, 5 subjects consumed dehydrated products, after storage for 1 year and exposure to 12,000 rad, for 70 days; concurrenlty 5 other subjects consumed the same foods, but they were not exposed to radiation. The fourth study involved 10 subjects and an analogous program, but with the use of foods after storage for 2 years and exposure to radiation in a dose of 24,000 rad. In the fifth study, 6 subjects consumed for 60 days dehydrated foods which, according to the results of the preceding studies, were recommended for rations for long-term space flights. In the last three studies, the subjects spent their free time in a specially reserved room under observation by medical personnel. Table 1 lists the characteristics of the diets. The diets were analyzed for levels of main nutrients and minerals. Each day, the subjects took 1 Undevit multiple vitamin lozenge. Fluid intake was not restricted, but a strict record thereof was kept.

Table 1. Nutrients contained in food rations (analytical data)

Study No.	Protein g/day	Fats g/day	Carbohydrate g/day	Calories, kcal/day
1	128	96	411	3100
2	131	125	344	3110
3	140	96	420	3200
4	140	96	420	3200
5	143	100	430	3280

The foods were dehydrated mainly by the freeze-dry method [5]. Some foods were dehydrated by heat drying. Development of the rations was made with the immediate participation of the All-Union Scientific Research Institute of the Food Canning and Vegetable Drying Industry under the USSR Ministry of the Food Industry. The subjects were under medical supervision, which involved physical examination, weighing, checking the pulse, body temperature and blood pressure. Peripheral blood was submitted to clinical analysis once every 10 days. Throughout the period of these studies the subjects rated the dishes and products on a 5-point scale. We examined the parameters characterizing protein, lipid, carbohydrate, vitamin, fluid-mineral metabolism, functional state of the adrenals and liver; we determined assimilation of the main nutrients and balance of a number of elements; we tested immunological reactivity of the body and composition of intestinal microflora. The results were submitted to processing by the method of variational statistics.

Results and Discussion

Throughout the 1st and 2d studies, the general well-being of the subjects was satisfactory. Pulse rate and arterial pressure did not exceed the range of physiological fluctuations. We failed to demonstrate pathological changes in morphology of peripheral blood. Weight loss was observed only in subjects who were significantly overweight with an initial weight of more than 75 kg.

In the 1st study, we found increase in general acidity and free hydrochloric acid in gastric juice. Subjectively, 4 out of 6 subjects reported varying degrees of heartburn for the first 2 months of the test. At the end of the 3d month, acidity of gastric juice began to diminish, and it returned almost to the base level by the end of the 4th month. These changes can be attributed to the process of adaptation of the digestive system to dehydrated foods [6]. In the 2d study, there was also a change in acidity of gastric juice, but it was inconsistent.

Total protein content of blood serum was in the normal range in both studies, and it differed insignificantly at different stages (7.5 to 8.1 g% in the first and 7.34 to 8.3 g% in the second). Electrophoregrams revealed an increase in albumin fraction in the 2d and 3d months of the first study ($P<0.05$). Concurrently there was a decrease in globulin concentration referable to the α- and β-fractions. By the 4th month of intake of the experimental ration, the levels of these fractions reverted to the background values [7]. There were insignificant changes in the blood serum proteinogram of subjects in the second study, and they did not exceed the range of physiological fluctuations. The similarity of results, indicative of absence of decrease in blood serum albumin fraction in both studies, enabled us to conclude that there was adequate protein intake, both qualitatively and quantitatively, on the experimental diets [8, 9].

In the first study, there was a decrease in concentration of most free amino acids of blood serum for the first 2-3 months of the period tested. The most marked decline was referable to glutamic acid, threonine, methionine and valine ($P<0.001$). In the 4th month, there was an increase in concentration of essential and nonessential amino acids. Evidently, the decline in level of free amino acids occurred as a result of poorer digestibility of proteins in dehydrated products by the proteolytic enzymes of the gastrointestinal tract. In the second study, we observed a decline of blood serum levels of some amino acids in different months.

Comparative analysis of the results of examining the end products of nitrogen metabolism revealed that excretion of total nitrogen, uric acid and creatinine in 24-h urine was at about the same level and within the physiological range in subjects participating in the first and second studies, whereas the nitrogen balance was close to zero or positive. These data are also indicative of the fact that the diets were satisfactory in protein content.

We failed to demonstrate appreciable changes in lipid metabolism (total lipids, α- and β-lipoproteins, total, esterified and free cholesterol) and vitamin metabolism (B_1, B_2, C, A, E and carotene). Blood sugar levels were in the physiological range [10] in both studies; fluid metabolism constituted 3005 mℓ in the first study and 2727 mℓ in the second, i.e., there was an average of about 1 mℓ fluid per kcal energy consumed. In the first study, we failed to demonstrate significant changes in balance of the main biogenous elements (N, P, Mg, S, K, Na, Cl), with the exception of Ca in the 3d and 4th months of the experimental period due to significant decrease in assimilation. In the second study, Ca content of the diet was increased from 0.82 to 1.27 g/day. The amount of minerals in the diet of subjects involved in the second study, including Ca, was sufficient to maintain the balance thereof in the body.

Assimilation of main nutrients from dehydrated foods was not lower than from analogous freshly prepared foodstuffs (Table 2).

Table 2. Assimilation of main nutrients in the diets, %

Nutrients	Study No									
	1		2		3		4		5
	diets									
	background	experi-mental	background	experi-mental	after 1-yr storage	after 1-yr storage and 12,000 rad radiation	after 2-yr storage	after 2-yr storage and 24,000 rad radiation	experi-mental
Proteins	88,6	88,3	90,0	90,6	88,0	86,0	87,0	89,0	90,0
Fats	93,4	96,6	95,1	97,5	96,4	96,8	97,0	97,0	97,0
Carbohydrates	96,1	95.0	98,0	96,6	97,8	97,4	96,0	96,0	97,0

The results of these studies enabled us to conclude that it is possible for man to stay on a diet consisting entirely of dehydrated foods for a long period of time (up to 1 year) [11].

Since radiation induces a number of changes in chemical composition of foods [12, 13], it was necessary to determine how the doses, spectrum of radiation and prolonged storage expected during a space flight would affect the biological value of dehydrated foods.

At first, we studied the biological value of the diet of rats exposed to γ-rays and protons in a dosage of 70,000 rad. It was shown that after being given the experimental diet for 6-7 months there were no appreciable changes in weight of the animals, weight of internal organs, peripheral blood, amino acid composition of blood serum, total protein and protein fractions, as well as levels of sugar, cholesterol, total lipids, lipoproteins vitamins E and B group in the rats' blood [14].

As a result of the third and fourth studies, it was established that most of the tested dehydrated foods retained their biological value, according to organoleptic, physicochemical, biochemical and bacteriological tests, and provided for a satisfactory nutritional status of the subjects after storage of food for 1 year and exposure to protons in a dosage of 12,000 rad, as well as after 2-year storage and exposure to up to 24,000 rad. The data in Table 2 are indicative of a high degree of assimilation of the diets of freshly prepared dehydrated foods [15]. Examination of gastric juice after termination of the studies of subjects with diminished gastric secretion revealed an increase to normal levels, whereas in subjects with normal and somewhat elevated gastric secretion the parameters remained in the range of initial values.

All of the foodstuffs and dishes contained in the experimental diets were entirely consumed by the subjects. The mean rating thereof was 4. As a result of these studies, determination was made of the list of dehydrated foods and dishes that were suitable for making up a diet, the adequacy of which with regard to plastic and energy requirements of man was tested in the fifth study.

At the first stage of this study, there was a tendency toward decrease in free amino acid content of blood plasma and a statistically reliable increase in amino nitrogen of urine ($P<0.01$). As in the first study, it may be assumed that there was retention of release and absorption of some amino acid due to the poorer digestibility of proteins in dehydrated foods by digestive system enzymes. As we know, an amino acid imbalance diminishes utilization of amino acids for protein synthesis, and it is associated with increased excretion of amino acids in urine [16].

Total protein content of blood serum, particularly albumins, diminished ($P<0.05$); this also applied to hemoglobin; these are the "mobile" protein reserves of the body, which diminish when there is insufficient delivery of amino aicds to tissues [9]. By the 45th day of the study, all of these parameters reverted to background levels, and this can be interpreted as adjustment of the subjects to the altered diet.

For 60 days, the experimental diet provided for a normal health status, good level of performance by the subjects; it did not induce appreciable changes in lipid, carbohydrate, fluid-mineral and vitamin metabolism. The parameters characterizing immunological reactivity of the subjects were also quite stable. The composition of a diet consisting of dehydrated foods for use during long-term space flights was defined and recommended on the basis of the results of these studies.

BIBLIOGRAPHY

1. Bychkov, V. P. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1967, pp 8-14.
2. Ordway, F.; Gardner, J. P.; and Scharpe, M. R. "Basic Astronautics," New York, 1968, p 587.
3. Bobkov, V. G.; Demin, V. P.; Keirim-Markus, I. B.; et al. "Radiation Safety During Space Flights," Moscow, 1964.
4. Bychkov, V. P.; Kozar', M. I.; Popov, V. I.; et al. KOSMICHESKAYA BIOL., No 3, 1974, pp 6-10.
5. Guygo, E. I., and Kaukhcheshvili, Ye. I. PISHCHEVAYA PROM-ST' [The Food Industry], No 1, 1963, pp 16-19.
6. Bychkov, V. P.; Kozar', M. I.; Korotayev, M. M.; et al. in "Aviatsionnaya i kosmicheskaya meditsina" [Aviation and Space Medicine], Moscow, Vol 1, 1969, pp 98-101.
7. Byckov, V. P.; Kozar', M. I.; Boyko, N. N.; et al. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 16, 1971, pp 254-269.
8. Gaurovits, F. "Chemistry and Biology of Proteins," Moscow, 1953.
9. Kremer, Yu. N. "Biochemistry of Protein Nutrition," Riga, 1965.
10. Bychkov, V. P. KOSMICHESKAYA BIOL., No 4, 1969, pp 17-23.
11. Ushakov, A. S.; Vysotskiy, V. G.; Bychkov, V. P.; et al. in "Simpozium po kosmicheskoy biologii i meditsine. 5-y [Fifth Symposium on Space Biology and Medicine], Warsaw, 1972, pp 107-112.
12. Kung, H. C.; Gaden, E. L.; and King, C. C. J. AGRIC. FOOD CHEM., Vol 1, 1953, p 142.
13. Metlitskiy, L. V.; Rogachev, V. I.; and Khrushchev, V. G. "Radiation Processing of Foodstuffs," Moscow, 1967.

14. Bychkov, V. P.; Kozar', M. I.; Markaryan, M. V.; et al. in "Gagarinskiye chteniya. Med. i biologicheskiye problemy kosmicheskikh poletov" [Gagarin Lectures: Medical and Biological Problems of Space Flights], Moscow, 1973, pp 13-17.

15. Bychkov, V. P., and Markaryan, M. V. Ibid, pp 18-33.

16. Mayster, A. "Biochemistry of Amino Acids," Moscow, 1961.

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SYSTEM OF HYGIENIC INSPECTION OF NONMETAL MATERIALS USED IN SPACECRAFT EQUIPMENT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 70-74

[Article by G. I. Solomin, submitted 3 May 78]

[English abstract from source]

In view of a wide use of polymers in the spacecraft interior and their potential hazard, a system of hygienic control over their safety at every manufacture stage has been introduced. The system includes: an analysis of a list of polymers; laboratory testing of samples under standard conditions; bench testing of various polymers used in the hardware and software under operational conditions; an examination of space cabin environments in real flights. The system of hygienic control allows selection of the safest polymers, i. e. those with minimum outgasing.

[Text] The conditions under which polymers are used in spacecraft differ significantly from all others, and they could affect the level of outgasing and, consequently, their toxicity [1-3]. For this reason, one of the pressing tasks is to study the long-term effect on materials of the main microclimate factors in a pressurized space: high temperature, humidity, air flow velocity, altered gas composition and low barometric pressure. In addition, at temperatures that are below those at which polymers are destroyed, there may be a linear dependence of outgasing on temperature level. At the time the destruction temperature is reached there is a sharp increase in outgasing, and this may be associated not only with a change in amount of released substances but a change in their composition. Lowering of barometric pressure to 258 mm Hg with concurrent change in gas composition of the environment in a sealed space lead to 3-4-fold increase in concentrations of chemicals. An increase in air humidity is also usually associated with an increase in concentration of volatile products in the gas phase. An increase in linear velocity of air above the polymer has a significant influence on the outgasing process. A higher level of trace impurities was found when the velocity of air above a polymer was increased to 0.15-0.20 m/s. Further increase in air velocity did not affect the rate of outgasing, which was determined only by the process of diffusion of low molecular substances in the polymer [4].

It was established that there is a proportionate dependence of outgasing on saturation for a number of porous, film materials, rubbers and adhesives. In the case of long-term storage of polymer samples in a sealed space (up to 7 months), there is an exponential decrease in discharge of chemicals [5].

All of the foregoing prompted development and scientific substantiation of a system of hygienic control for the safe use of nonmetal materials used in the equipment of manned pressurized cabins of spacecraft. The system of hygienic inspection [control] that exists at the present time involves the following: screening of materials that do not release volatile products or present minimal outgasing when exposed to a temperature of 40°C; sanitary-chemical and toxicological testing of outgasing products from materials that were previously not examined in the laboratory and about the safety of which there is no information; development of steps to diminish outgasing (methods of hygienic "refinement"); development of recommendations pertaining to creation of heat-stable materials by improving the technology of their production, search for nontoxic raw material and additives; investigation of products of outgasing in the air environment of pressurized compartments.

Hygienic inspections are performed in the following manner, in accordance with the stages in construction of spacecraft:

1) primary analysis of the list of nonmetal materials used in a given item; 2) laboratory testing of each sample individually under standard conditions (saturation 1 kg, 1 g, 1 m^2, 1 pm per m^3 volume; temperature 40°C; barometric pressure 760 mm Hg; relative humidity 60-70%) or with specified parameters of the environment; 3) bench testing of different groups of materials under specified operating conditions; 4) mockup testing of the entire aggregate of nonmetal materials used under conditions that are as close as possible to real ones; 5) identification of products of polymer outgasing and quantitative assay thereof in the air of manned compartments of spacecraft in the course of flights.

The objective of hygienic analysis of the list of nonmetal materials is to screen samples for further investigation at the stage of laboratory testing, as well as to determine the entire scope of subsequent studies with due consideration of the target date for construction of the unit. Materials having no toxicological significance (wood, paper, etc.), as well as polymers contaning substances referable to the class of extremely toxic compounds (overt allergens, carcinogens, mutagens, etc.) are not submitted to study at the laboratory test stage. The latter materials are generally banned from use in pressurized compartments. Moreover, in the case of low saturation of a material (up to 100 cm^2/m^3 or less than 1.0 g/m^3) and low operating temperature (up to 40°C), the question of necessity for sanitary and chemical tests can be settled on the basis of certificate data concerning the composition of polymer material and technology of its manufacture. When examining the list of materials, such indices as presence of GOST or technical conditions are taken into consideration. Use of experimental samples is permitted in exceptional cases and then only after they have been submitted to the complete schedule of examination.

At the second stage of hygienic control, experimental sanitary-chemical and, when necessary, toxicological studies of each sample individually are made. In view of the fact that there is a rather large volume of work at this stage, use of high-speed express methods for testing materials is justified [6, 7]. Hygienic evaluation on the basis of the results of sanitary chemical analysis is made by comparing outgasing levels referable to the different chemicals to their maximum permissible concentrations (MPC) in the air of sealed compartments. Due consideration is given to the nature of the expected combined effect by means of demonstration of substantces that have effects in the same direction. In those cases when a material discharges several toxic substances with the same direction of action, each of which is at the level or below the relevant MPC, determination is made of the overall index of the demonstrated concentrations in relation to their MPC. If the overall index does not exceed or equals 1, the material can be given a preliminary positive rating [8].

Studies of more than 500 polymer materials in the laboratory revealed that about 100 names of chemicals were identified in the process of gas chromatographic analysis of the products of outgasing of various polymers [9]. As a result of the studies, it was established that chemical compounds referable to saturated, unsaturated and aromatic hydrocarbons, aldehydes and alcohols are encountered the most frequently in the gas complex. Paints, varnishes and enamels emit the most gases (up to 80%). The levels of demonstrated concentrations most often constitute 0.9-0.01 mg/m^3. However, equiponderant concentrations of different components may constitute up to tens of milligrams per m^3. Toxicologically, the gas complexes should be considered as a low intensity factor.

Thus, the objective of work done at the stage of laboratory testing is to screen samples of materials with the lowest outgasing level, i.e., to obtain data concerning their relative toxicity.

At the stage of laboratory testing, odorimetric tests are also performed if necessary. Materials with a distinct odor are not recommended, since we know that substances capable of stimulating the receptors of the nose and upper respiratory tract induce, in addition to a sensation of odor or irritation, several undesirable reflex reactions, which alter the rate and amplitude of respiratory excursions, tonus of blood vessels, induce nausea, etc.

The bench tests are conducted on different groups of materials which are most often components of diverse equipment and instruments. In these tests it is possible to reproduce and maintain for a long time any specific operating conditions. Reproduction of specified conditions makes it possible to obtain the most objective information about the nature of emission of volatile substances, as well as to determine the degree of their possible effects on animals and man.

Numerous studies at the bench test stage revealed that the levels of chemicals emitted by a group of materials do not reach the levels of overall concentrations of the same substances demonstrated in the laboratory for individual polymers. This phenomenon is attributable to a number of factors, and in particular to the "shielding effect," which arises because of the reciprocal location of polymers in products and equipment. The reciprocal influence of materials on the outgasing process is manifested by a significant decrease in concentrations of the different products discharged by each of the tested samples individually, while a number of components are not demonstrable at all in such cases [10]. Moreover, it was established that some of the water-soluble compounds migrate into the condensate of atmospheric humidity [11].

A special device was developed for toxicological studies of the possible deleterious effects of polymer outgasing products, and it permits testing in a closed space [2]. When examining the functional state of animals, use is made of both integral indices characterizing the gas complex as a whole and specific tests for demonstration of the toxic effects of the main components, as well as functional load methods which make greater demands of the organism.

The fourth stage of examination of materials involves a number of mockup tests, including some with the participation of man, where the entire aggregate of polymers is used that had undergone prior examination under conditions that were as close as possible to actual ones. These tests include examination of air in the mockup with the use of heat tests. Here, determination is made of pollution of the air environment of manned pressurized compartments by polymers. It is important and mandatory to test the life support systems; in the course of these tests studies are made of the efficacy of regular [standard] systems of air purification, as well as complex medical studies of the air environment as a whole with due consideration of human gas emission. In the mockup tests, a complex evaluation is made of polymers, including other expected effects: presence and level of static electricity, biostability of polymers, dust content of air, etc. The results of the mockup tests revealed that the number of trace impurities discharged by polymers is up to 20-30. Many of them are the products of human gas emission. The volatile products include saturated, unsaturated and aromatic hydrocarbons, aldehydes, ammonia, carbon monoxide, acetates, alcohols, acetone, organochlorine compounds in concentrations at levels that are permissible for the air of pressurized compartments.

In conclusion, it must be noted that introduction of a scientifically substantiated system of hygienic supervision of safe use of polymers made it possible to lower significantly the level of outgasing in manned compartments of spacecraft. At the same time, experience in hygienic rating of materials shows that, with the every increasing duration of space flights, one should expand comprehensively the work pertaining to screening of the best materials, from the toxicological point of view, as well as development of stable, heat-resistant polymers. It is also imperative to try to limit the use of a wide diversity of synthetic materials, to standardize them, to make more use of methods of preliminary "refinement" of polymers that discharge toxic impurities and, at the same time, to search for methods of effective purification of the air in pressurized compartments.

BIBLIOGRAPHY

1. Gazenko, O. G., and Genina, A. M. (editors) "Chelovek pod vodoy i v kosmose" [Man Under Water and in Space], Moscow, 1967.
2. Solomin, G. I. in "Aviatsionnaya i kosmicheskaya meditsina" [Aviation and Space Medicine], Moscow, Vol 2, 1969, pp 224-227.
3. Sopikov, N. F.; Gorban', G. M.; Bizin, Yu. P.; et al. Ibid, Vol 3, pp 24-30.
4. Sopikov, N. F.; Yablochkin, V. D.; Shchirskaya, V. A.; et al. Ibid, pp 31-38.
5. Gorshunova, A. I., and Chukhno, E. I. in "Aktual'nyye voprosy kosmicheskoy biologii i meditsiny" [Pressing Issues of Space Biology and Medicine], Moscow, Vyp 1, 1971, pp 89-93.
6. Demchenko, Ye. A.; Chukhno, E. I.; Gorshunova, A. I.; et al. in "Aktual'nyye problemy kosmicheskoy biologii i meditsiny" [Pressing Problems of Space Biology and Medicine], Moscow, Vol 1, 1977, pp 10-11.
7. Popov, A. M. in "Aviatsionnaya i kosmicheskaya meditsina," Moscow, Vol 3, 1969, pp 20-24.
8. Gorban', G. M., and Solomin, G. I. in "Mediko-tekhnicheskiye problemy individual'noy zashchity cheloveka" [Medicotechnical Problems of Personal Protection], Moscow, Vyp 10, 1972, pp 39-44.
9. Yablochkin, V. D. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1975, pp 27-30.

10. Yablochkin, V. D.; Korostyleva, Ye. A.; Gorshunova, A. I.; et al. in "Kosmicheskaya i aviakosmicheskaya meditsina" [Space and Aerospace Medicine], Moscow--Kaluga, Vol 1, 1972, pp 240-243.

11. Bizin, Yu. P.; Gorban', G. M.; Zinov'yev, V. M.; et al. in "Aviatsionnaya i kosmicheskaya meditsina," Moscow, Vol 3, 1969, pp 3-7.

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STUDY OF COMPATIBILITY OF CERTAIN HIGHER PLANTS AND CHLORELLA AS RELATED TO A BIOREGENERATIVE HUMAN LIFE SUPPORT SYSTEM

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No 2, 1980 pp 74-78

[Article by Yu. I. Shaydorov, B. N. Shebalin and G. I. Meleshko, submitted 15 May 78]

[English abstract from source]

The phototrophic component of a bioregenerative life support system should be of a multispecies structure. It should incorporate not only higher plants but also different algae. The paper discusses the studies concerning mutual effects of Chlorella and higher plants cultivated together in a closed atmosphere. It can be inferred from the studies that gaseous products of Chlorella did not exert a significant effect on the carbon dioxide consumption by wheat and radish plants or on their biomass increment. In turn, gaseous products of higher plants did not influence Chlorella growth. It can, therefore, be concluded that Chlorella and the above higher plants, when cultivated in a common atmosphere, do not inhibit each other and can be regarded as biologically compatible constituents of the photoautotrophic component of future bioregenerative life support systems.

[Text] The photoautotrophic elements of future bioregenerative life support systems should have a multispecific structure. According to the established opinion, the photoautotrophic element should include, along with higher plants, various forms of unicellular algae. The unquestionable superiority of higher plants from the standpoint of nutrition would thus be combined with the high technological effectiveness and controllability of unicellular algae [1].

The great stability of natural biocenoses is indicative of the presence in them of informative-controlling relations between the forms of organisms of which they consist. One of the mechanisms of such connections is the direct link via metabolic products released into the common environment they inhabit. Investigation of the reciprocal influence by means of released metabolites is a mandatory prerequisite for developing closed bioregenerative human life support systems, in which the direct correlations between components are known to be more marked than under ordinary conditions, because of the restricted space and specific amount of inert environment.

Cultivation of higher plants and chlorella in a human life support system that was closed for gas exchange did not yield an unequivocal answer to the question of compatibility of the components studied [2].

At the same time, microalgae and higher plants can be classified in groups of organisms that are evolutionarily interdependent, since algae are always present under natural conditions in the rhizospheric and root zones of higher plants, and there are usually more algae in the plant rhizosphere than in the soil around them, which is indicative of the symbiotic nature of their correlations [3, 4].

Our objective here was to study the reciprocal influence of chlorella and certain representatives of higher plants when cultivated in the same atmosphere of a closed system. In order to demonstrate better the reciprocal influence by means of discharge of gases, one must increase the concentration of such discharges, determine the conditions of combining chlorella and higher plants with respect to carbon dioxide content in the atmosphere and to prolong their joint cultivation. The first requirement is met by having a small volume of air per unit biomass. As we know, the optimum concentrations of carbon dioxide are not the same for chlorella and higher plants, and they differ by a factor of 10. For this reason, we first studied the correlation between concentration of carbon dioxide in the atmosphere and rate of its uptake by wheat plants in the ranges of 0.1-0.5, 0.5-1.0, 1.0-1.5 and 1.5-2.0%, with oxygen content of 20.6 to 22.0%. We tested carbon dioxide uptake in each of the above ranges for 24 h. As shown by the results of our experiments, with increase in concentration of carbon dioxide from 0.1 to 0.5% there is increase in rate of its uptake. Further increase in concentration of carbon dioxide up to 20.0% did not have an appreciable effect on rate of uptake by plants. It must be stressed that this function, like all of the subsequent ones, was obtained when plants were cultivated with continuous illumination.

The duration of continuous joint cultivation of plants and algae is determined by the range of concentrations of oxygen and rate of build-up thereof in the system's atmosphere, within which no inhibitory effect is observed of an excess or shortage thereof on the process of photosynthesis. The intensity of carbon dioxide uptake by chlorella is directly related to the concentration of oxygen in the gas phase: with increase in content thereof there is decrease in intensity of photosynthesis [5]. The top range of oxygen content in the atmosphere constitutes 23-25% for a number of vegetable plants [6], while the bottom range is 2.5-5.0% [7]. There are also data to the effect that the influence of concentration of oxygen on photosynthesis of higher plants depends on cultivation conditions. For example, it was shown that lowering the temperature and increasing the concentration of carbon dioxide attenuate the inhibitory effect of high concentrations of oxygen. For this reason, we first determined the rate of carbon dioxide uptake by the plants studied as a function of oxygen and carbon dioxide content in the atmosphere.

Within the tested range, oxygen content did not have an effect on uptake of carbon dioxide by both plant species (Table 1, Figure 1).

Table 1. Rate of CO_2 uptake by wheat plants with different concentrations of oxygen and carbon dioxide in the atmosphere

Level in atmosph., %		Uptake of CO_2, ℓ/day
O_2	CO_2	
10—12	0,5—1,0	3,03±0,09
10—12	1,5—2,0	3,55±0,19
20—22	0,5—1,0	2,77±0,09
20—22	1,5—2,0	3,11±0,14

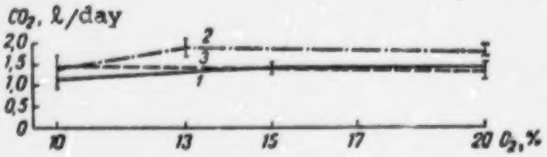

Figure 1.
Rate of CO_2 uptake by radish plants with different concentrations of oxygen in the atmosphere
1) 10-15-day-old plants
2) 15-20 day-old "
3) 20-25 " " "

Thus, the demonstrated dependence of intensity of photosynthesis on carbon dioxide content in the atmosphere enabled us to determine the range of its concentrations that would provide for normal vital functions of both the higher plants and chlorella when raised in the same atmosphere. The absence of effect of low oxygen concentration on photosynthesis of higher plants made it possible to prolong significantly the time of continuous joint cultivation of the components studied in the same atmosphere without partial or total replacement thereof.

Methods

The study of mutual influence of higher plants and chlorella was pursued on an installation, the diagram of which is illustrated in Figure 2.

This installation consists of a microalgal reactor with receiver and three pressure chambers for higher plants, one of which was combined with the reactor into one gas line, while the other two served as a control. The chambers and reactor are equipped with the necessary systems and devices for prolonged continuous cultivation of plants, measurement and regulation of the main parameters, both in autonomous and combined modes. In each chamber, the planting area constituted 0.1 m^2 and air volume was 60 ℓ. The volume of algal suspension constiututed 1 ℓ, with 0.15 m^2 illuminated reactor surface. Overall air volume of the system was 90 ℓ, illumination of plants and the suspension constituted 100 W/m^2 FAR [expansion not known].

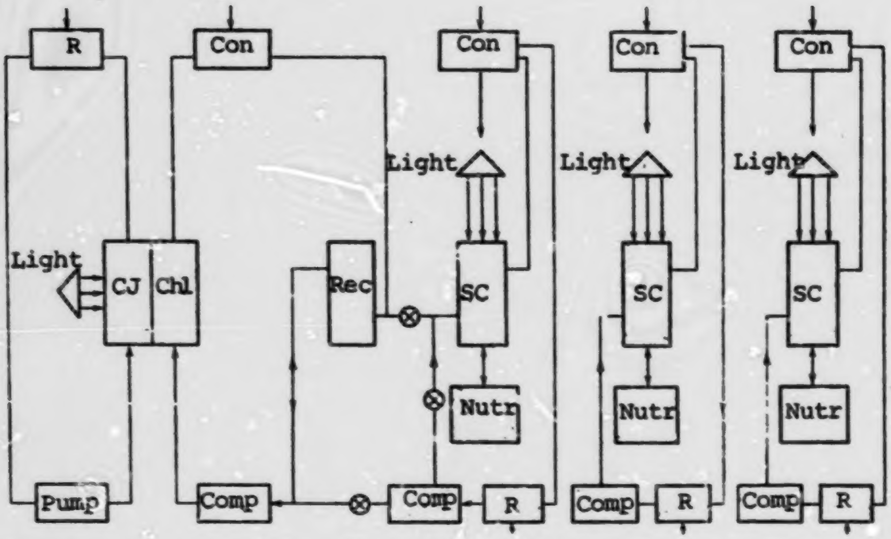

Figure 2. Diagram of installation. Explanation given in the text.

Key:
R) refrigerator
Con) condenser
CJ) cooling jacket
Rec) receiver
SC) sealed [pressure] chamber for higher plants
Nutr) nutrient solution
Chl) chlorella
Comp) compressor

In the tests, we used Strela spring wheat plants, pinkish-red radish and chlorella (Chlorella Sp-k). Up to the age of 19 days, the wheat plants were raised in an open device, then put in the pressure chamber, where they remained up to the age of 36 days. At this time (from the age of 20 to 36 days) biomass increment was relatively constant, constituting about 3 g dry substance per 100 plants per day. Radish seedlings were also kept in the open installation up to the age of 10 days, then put in the sealed chamber where they continued to grow to the age of 28 days. The concentration of carbon dioxide was held at 1 to 2% and oxygen at 10 to 22%. Before placing the components under study in the same gas line [system], we studied the intensity of carbon dioxide uptake and oxygen output by chlorella and the higher plants when raised under autonomous conditions. Wheat and chlorella were held in the same atmosphere for 3 days. Overall duration of joint cultivation of radishes and chlorella was 17 days. We lowered oxygen content every 3 days to 10% by pumping nitrogen through the system. We studied the effect of the common atmosphere not only on plant growth, but their development. In all of the experiments we conducted, along with examination of gas exchange in the system we determined chlorella productivity according to biomass increment.

Results and Discussion

Joint cultivation of chlorella and wheat in the same atmosphere did not affect their uptake of carbon dioxide, and photosynthesis of both components in the autonomous mode of cultivation did not change after cultivation in the same atmosphere (Table 2). The obtained data characterize photosynthesis and growth of wheat plants only for the tested period of time, during which the plants were at the same phase of development.

Table 2. Rate of carbon dioxide uptake by chlorella and wheat plants in the case of autonomous and joint cultivation in the same atmosphere

Cultivation	Chlorella		Wheat	
	cultiv. time, h	CO_2 uptake, ℓ/day	cultiv. time, h	CO_2 uptake, ℓ/day
Autonomous	4,0	2,88±0,12	14,5	3,16±0,17
Joint	42,0	2,96±0,54	42,0	3,18±0,62
Autonomous	7,5	3,24±0,13	7,5	2,61±0,17
Joint	11,5	3,12±0,11	11,5	3,07±0,11
Autonomous	13,0	3,04±0,58	13,0	2,53±0,37

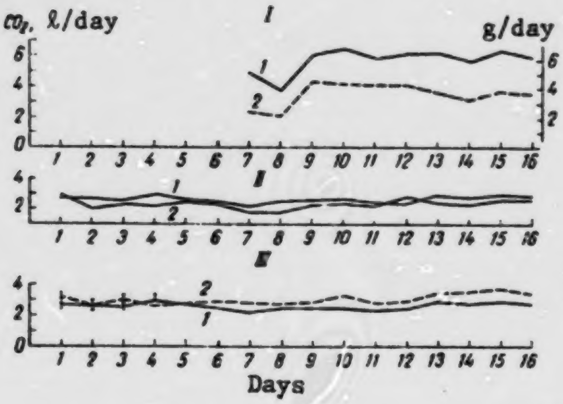

Figure 3.
CO_2 uptake by radish and chlorella with autonomous and joint cultivation in the same atmosphere
I) overall CO_2 uptake by radish and chlorella (1) and chlorella productivity in autonomous mode (2; g/day)
II) CO_2 uptake by radish plants with with autonomous cultivation in chamber No 3 (1) and No 2 (2)
III) CO_2 uptake by radish plants when cultivated autonomously (1) and jointly with chlorella in the same atmosphere (2)

Figure 3 illustrates the mean daily uptake of carbon dioxide by chlorella and radish plants when cultivated together, as well as productivity of chlorella according to dry substance increment. Overall uptake of carbon dioxide coincided entirely with the trend of the curve of productivity of chlorella according to dry substance. Analysis of the data illustrated in

Figure 3 shows that uptake of carbon dioxide by radish plants raised in the same atmosphere as chlorella was virtually the same as when raised autonomously. Phenological observations of growth and development of radish plants cultivated in the same atmosphere as chlorella and under autonomous conditions failed to demonstrate any substantial changes in development. We only observed earlier bolting (by 1-2 days) of experimental plants.

After the experiment, we measured plant weight and determined the structure of the level. Wet and dry biomass of radish plants raised under autonomous conditions and in the same atmosphere with chlorella was virtually the same (the differences were unreliable).

In view of the fact that the plants had started to bolt intensively at the time they were harvested, growth of the root crop was retarded in both the experiment and control, and this is probably related to the fact that there was continuous illumination.

The results of these experiments allow us to conclude that under our test conditions gas discharge by chlorella did not have an appreciable effect on uptake of carbon dioxide by wheat and radish plants or on their biomass increment. In turn, the gas discharge of higher plants did not affect vital functions of chlorella. Consequently, we can voice the preliminary conclusion that chlorella and the representatives of higher plants studied do not have an appreciable reciprocal inhibitory effect when cultivated in the same atmosphere, and for this reason they may be considered as biologically compatible components of the photoautotrophic element of future bioregenerative human life support systems.

BIBLIOGRAPHY

1. Shepelev, Ye. Ya.; Meleshko, G. I.; and Sidorenko, L. A. in "Chteniya, posvyashchennyye razrabotke nauch. naslediya i razvitiyu idey K. E. Tsiolkovskogo. 6-ye. Trudy" [Lectures Dealing With Development of the Scientific Legacy and Ideas of K. E. Tsiolkovskiy, 6th Series], Moscow, 1972, p 33.

2. Terskov, I. A.; Gitel'zon, I. I.; Kovrov, B. G.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1974, p 33.

3. Shtina, E. A. TRUDY KIROVSK. S.-KH. IN-TA [Works of the Kirov Agricultural Institute], Vol 2, No 23, 1956, p 33.

4. Idem, VESTN. MOSK. UN-TA [Vestnik of Moscow University], No 6, 1956, p 93.

5. Idem, NAUCH. DOKL. VYSSH. SHKOLY. BIOL. NAUKI [Scientific Reports of Schools of Higher Learning, Biological Sciences], No 1, 1960, p 75.

6. Meleshko, G. I.; Antonyan, A. A.; Kazakov, A. I.; et al. KOSMICHESKAYA BIOL., No 2, 1973, p 41.

7. Nilovskaya, N. T., and Bokovaya, M. M. FIZIOLOGIYA RASTENIY [Plant Physiology], Vol 15, No 2, 1968, p 258.

8. Ostaplyuk, Ye. D.; Kurochkina, A. L.; and Cherkavskiy, O. F. FIZIOLOGIYA I BIOKHIMIYA KUL'TURNYKH RASTENIY [Physiology and Biochemistry of Cultivated Plants], Vol 7, No 4, 1975, p 360.

METHODS

UDC: 616.28-07:617.761-009.24

GENERALIZED NYSTAGMOMETRIC CHARACTERISTICS FOR DIAGNOSTIC PURPOSES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 78-82

[Article by M. M. Levashov and A. I. Tumakov, submitted 4 Apr 78]

[Text] Nystagmometric diagnostics amount to comparing "output" reactions induced by the same perturbances at the "input" of the system studied. It is assumed that there is a certain "norm" (or background), a difference from which is evaluated as a sign of pathology (or influence of a factor studied).

In most cases, the comparison is made by assessing the probability of error made when relating the compared reactions to various sets. It is not always by far that the changes in nystagmus, when assessed according to a single parameter, are statistically significant and reliably beyond the range of normal variations. Yet we know that deviations may consist not only of a significant change in some nystagmometric characteristics, but change in correlation between parameters. In other words, there may be impairment of correlations, according to which one can demonstrate a reliable deviation of reactions from normal, although each of the parameters individually would not differ from the norm.

Generalized evaluation of the nystagmic reaction (or reactions), which takes into consideration the statistical relationship between parameters of nystagmus [1-3], could be used as the basis for solving the problem of demonstrating such differences. It was proposed that the so-called distance (quadratic form of deviation of random [sampled] values of parameters from the corresponding means) be used as a gage of deviation from the norm. One can judge not only the reliability of a difference (i.e., probability of erroneous judgment), but trends in direction of changes in repeated tests, if necessary, according to this distance. Two approaches have been developed, which differ in their concrete objectives. In the first case (first type of diagnostics), a "normal" set of nystagmograms is described, in which each individual reaction is presented as a generalized evaluation of two or more parameters (for example, three-dimensional distribution, which is constant for duration of nystagmus, mean rate of slow component and mean frequency). An individual nystagmic reaction, which must be given a diagnostic evaluation is compared to this distribution, i.e., determination is made of the reliability of its difference at a specificed confidence level [1, 4]. In the other case (second type of diagnostics), it is not an individual nystagmic reaction that is the object of diagnosis, but a pair of reactions recorded on a subject, for example in the same caloric test on the right and left. In this case, the generalized evaluation takes into consideration the statistical relations existing between analogous parameters in reactions going in different directions. Accordingly, the norm (or background) is a sample, in which each date is represented by a pair of reactions, while the distance, which serves as a gage of difference, indicates the extent to which a given subject differs from the "norm" with regard to the sign of correlations between analogous parameters of reactions elicited by the same stimulation of different labyrinths. As related to cold caloric nystagmus, this procedure of nystagmometric diagnostics (statistics of the norm, conversion of initial samples, formula for calculation of distance, deciding diagnostic rule) was described comprehensively before [1].

Our objective here was to demonstrate the possibility and prospects of using the second type of diagnostics for the purpose of evaluating optokinetic reactions. Optokinetic nystagmus (OKN), which has long been an object of investigation in special diagnostic studies [5], is acquiring increasing significance in vestibulometric studies as its close links with the vestibular system are being demonstrated [6-8]. Evidently, recording and quantitative evaluation of OKN will become mandatory elements of the vestibulometric diagnostic complex used in occupational screening in the very near future. For this reason, it is a pressing task to determine the deviations of OKN from normal, including asymmetries, i.e., to demonstrate pathological asymmetry beyond the range of physiological asymmetry, which is not uncommon. Moreover, we should like to call the reader's attention to a convenient graphic procedure, with which calculations involved in the second type of diagnostics can be simplified.

Methods

We studied 39 children ranging in age from 3 to 7 years who were not suffering from vestibular dysfunction. The methods and detailed description of examining them were described previously [3]. The optokinetic stimulus (white spots of the same size randomly scattered on a black background), which moved in the horizontal plane, was projected on a screen that occupied a significant part of the field of vision (120° horizontally and 70° vertically). The subjects were merely asked to look at the screen, and no other instructions were given. We submit below the results of processing 234 electronystagmograms (ENG) of OKN recorded at three stimulus rates, 4, 10 and 20°/s. Primary processing of the ENG consisted of finding 2 characteristics for each reaction on a 20-s segment: the mean rate of the slow component (RSC) and number of jerks [beats]. The number of jerks measured in such segments corresponds to a 20-fold increased mean frequency, and for this reason we call this parameter the frequency in the tables and charts. Further processing was performed on an M-4030 computer. Each sample consisted of 39 pairs of analogous characteristics (for example, RSC) obtained in left and right OKN at the same stimulus rate. Thus, we obtained 6 samples (RSC and frequency with three stimuli) and for each of them we plotted joint distribution [1], determined the coefficients for the formula of quadratic deviation (i.e., distance) and 95% confidence interval fcr the norm (illustrated graphically).

We consider it necessary to mention that one should examine the norm (or background in each specific instance as related to the methods and other distinctions of the study, and it is expressly from this point of view that one should approach the norm described below. Further, the OKN norm for a child is unquestionably different from that of an adult. In this respect, our report may be of interest, not only as an example of an untraditional nystagmometric approach, but in connection with some of the distinctions of the OKN of children. It is known that the quantitative characteristics of OKN are substantially related to the extent to which the subject actively participates in visual tracking. An adult can be instructed to attentively examine a moving stimulus or, on the contrary, his attention can be distracted from tracking. We then obtain two qualitatively and quantitatively different OKN: the parameters of the second OKN depend much less on higher levels of the central nervous system, which correct eye movements and make the RSC conform with the speed of the stimulus. In addition, this nystagmus is more susceptible to influences of the vestibular system. It appears that in children, under the conditions of the methods we used, the reactions were closer to the second type of OKN.

Results and Discussion

The Table lists the results of traditional statistical processing (mathematical expectation and standard deviation (for the parameters of right (X) and left (Y) optokinetic reactions, as well as a sample made up of differences in parameters obtained for each pair of reactions. We also listed the coefficients of correlation ($r_{X,Y}$) between sets [samples] X and Y. To avoid ambiguity, let us indicate that the result of individual measurement of one OKN (for example, mean RSC of a right OKN) is designated as X, therefor X is the mean of the means. The same applies to reactions directed to the left. In the Table, we also list the coefficients of regression $R_{Y/X}$ and free terms of regression equations $B_{Y/X}$. The three coefficients (*a*, *b* and *c*) in the last columns of the table are referable to "second type of diagnostics," which we shall discuss below.

It is noteworthy that there is a distinct difference in behavior of two parameters of nystagmus, RSC and frequency. A significant positive correlation between left and right OKN was demonstrated with all three stimuli with regard to frequency, whereas a marked correlation for RSC was demonstrated only with a stimulus of 10°/s; it was insignificant with 20°/s and lacking with 4°/s. In other words, the rate of the optokinetic stimulus had a different effect on the tonic and rhythmic systems of nystagmus.

The quadratic deviation of distance for two-dimensional distribution was calculated with the following formula:

$$d = a\Delta_1^2 + b\Delta_1\Delta_2 + c\Delta_2^2$$

where Δ_1 is the difference between the value of the parameter studied in right OKN and corresponding mathematical expectation, Δ_2 is the same for left OKN in the subject examined, while a, b and c are the coefficients listed in the table for each of six samples made up of pairs of characteristics. These coefficients were obtained as a result of converting the initial paired OKN samples to apply to the second type of diagnostics [6].

Main statistics of OKN samples at three rates of optokinetic stimulus

Stimulus, degrees/s	$\overline{X}$	$\overline{Y}$	$(\overline{X}-\overline{Y})$	$r_{X,Y}$	$R_{Y/X}$ $B_{Y/X}$	a	b	c
				RSC				
4	4,23	4,33	—0,055	—0,178*	—0.196	1,546	0,502	1,280
	(0,82)	(0,90)	(1,318)		5,147			
10	10,85	11,04	—0,192	0,753	0,692	0,487	—0,799	0,587
	(2,18)	(2,00)	(1,477)		3,540			
20	20,52	20,59	—0.067	0,341	0,447	0,402	—0,210	0,236
	(1,68)	(2,19)	(2,257)		11,426			
				Frequency, number of jerks				
4	5,26	5,72	—0,462	0,890	1,311	1,070	—1,293	0,493
	(2,12)	(3,13)	(1,570)		—1,175			
10	14,59	14,51	0,077	0,829	0,773	0,082	—0,145	0,094
	(6,25)	(5,83)	(3,557)		3,235			
20	22,79	22,41	0,385	0,768	0,819	0,035	—0,050	0,030
	(8,37)	(8,93)	(5,923)		3,734			

Note: Standard deviations of samples are given in parentheses; the asterisk indicates an unreliable difference from zero.

We must make several simple calculations to determine whether a pair of the subject's reactions differs from the "norm" with regard to the sign of correlations between analogous parameters of these reactions. We have to find the mean RSC and number of jerks per 20-s segments of the reactions in each of two ENG of the subject's OKN recorded with the same stimulus rate. We then have to calculate Δ_1 and Δ_2 as the difference between the obtained values and corresponding mathematical expectations. For example, Δ_1 equals (if the evaluation pertains to RSC) the difference between mean RSC of the subject's right OKN (X) and arithmetic mean of RSC of the right OKN with a given stimulus (i.e., $\bar{X}$, see Table). The values found for Δ_1 and Δ_2 with the corresponding coefficients, which are listed in the Table, must be substituted in the formula, and then d is calculated (distance). With $d \geqslant 6.0$, the probability of error in referring the pair of OKN to those differing from normal would constitute less than 5%.

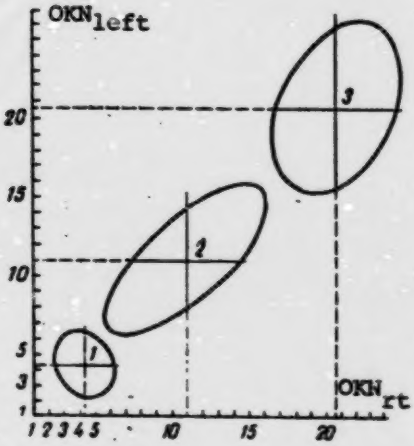

Figure 1.
Rate of slow component of OKN (mean RSC for 20-s segment of OKN) with different rates of optokinetic stimulus. Generalized characteristics are given for three samples each consisting of 39 pairs of analogous parameters in differently directed reactions (x-axis, SRC for right OKN; y-axis SRC for left OKN). Here and in Figure 2, the ENG's were plotted for three stimulus rates: 4 (1), 10 (2) and 20°/s (3). The straight lines refer to coordinates of mathematical expectation, the oval circumscribed zones refer to 95% confidence level in each sample.

If there is no need to know the exact value of d (for example, when it is sufficient merely to determine that it differs from "normal"), one can use the graphs illustrated in Figures 1 and 2. After finding the point of intersection of coordinates for the parameters of a pair of reactions in a given subject, one can make a diagnostic decision according to the location of this point, in or out of the zone circumscribing a 95% confidence level. Whenever the point is outside this zone, the decision is made that the tested pair of OKN differs reliably ($P<0.05$) from the "norm." This procedure may be particularly useful in mass screenings, since it makes it possible to do without making calculations using the formula.

This procedure may also be useful in selecting an optimum examination and informative parameters of the reaction. Thus, the stimuli we used apparently differ in significance to the system under study. This is indicated, for example by the dependence of the individual physiological RSC asymmetry on the rate of the stimulus. Let us explain this with an example. Since the position of any point of intersection of the coordinates, which does not exceed the boundaries of the circumscribed zone must be interpreted as a sign that it belongs to a normal set, let us find in each zone a point, for which X and Y will differ enough, i.e., let us find reactions that are in the normal range and,

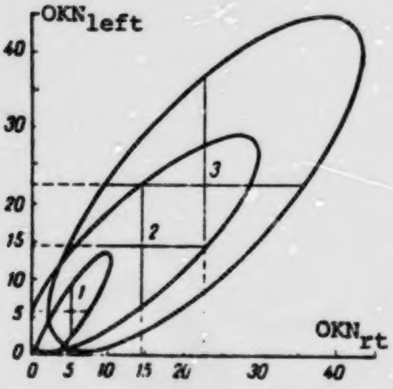

Figure 2.
Frequency of OKN (jerks per 20-s OKN) at different rates of optokinetic stimulus. Generalized characteristics are given for three samples (x- and y-axes, right and left OKN, respectively)

at the same time, asymmetrical for RSC. With a stimulus of 4°/s, we can select a point with coordinates X = 2.5 and Y = 5.0. The absolute difference in RSC in such a pair of OKN will be 2.5°/s, and the relative difference, expressed as percentage of sum of RSC, will reach -33%. Analogously, let us evaluate a pair of reactions with a stimulus of 10°/s: at the point with coordinates X= 5.5 and Y = 7.5, the absolute difference will be -2.0°/s and relative difference -15%. With a stimulus of 20°/s, at the point with coordinates X = 16.5 and Y = 19, where the absolute difference is -2.5°/s, the relative difference is -7.3%. In other words, as we move from low rate of stimulus (4°/s) to the highest (20°/s) there is an appreciable decrease in "normally" permitted relative asymmetry of OKN referable to RSC; for each distribution there is its own maximum level asymmetry. It is another matter for frequency (see Figure 2). Here, the point with coordinates of, for example, X = 3.0 and Y = 5.5 belongs to an equal extent to all three distribution; in such a pair, the relative frequency asymmetry will be -29%, i.e., quite significant asymmetry is "normal" for OKN evoked by any of the three stimuli.

Hence, it is better to use evaluation according to RSC, rather than frequency, whenever the object of the study is asymmetry of reactions, and of the stimuli used, the most advantageous will be the one with a rate of 20°/s, since physiological asymmetry is minimal with this rate. The distribution of RSC is less variable than distribution of frequency; for this reason, the frequency is not a very suitable parameter for assessing OKN asymmetry. Its variability is so significant that all three zones of 95% confidence level are superimposed over one another. These data compel us to adopt a cautious attitude toward diagnostic tests based only on evaluation of frequency. This suggests the practical conclusion that a comprehensive evaluation must be made of nystagmic reactions when there are problems related to diagnostics, i.e., mandatory consideration of properties of these reactions due to both rhythmic and tonic systems [9].

BIBLIOGRAPHY

1. Levashov, M. M.; Rodionov, V. D.; and Starostenko, A. M. in "Sensornyye sistemy. Vestibulyarnaya funktsiya" [Sensory Systems. Vestibular Function], Leningrad, 1974, pp 15-72.

2. Levashov, M. M.; Rodionov, V. D.; and Starostenko, A. M. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 4, 1974, pp 513-523.

3. Tumakov, A. I., and Levashov, M. M. in "Voprosy fiziologii i patologii slukhovogo i vestibulyarnogo analizatorov" [Problems of Physiology and Pathology of Auditory and Vestibular Analyzers], Moscow, 1977, pp 82-86.

4. Levashov, M. M.; Rodionov, V. D.; and Starostenko, A. M. AGRESSOLOGIE, Vol 16, 1975, pp 175-178.

5. Blagoveshchenskaya, N. S. "Electronystagmography in Focal Brain Lesions," Leningrad, 1968.

6. Babiyak, V. I. "Oculomotor Reactions and Their Sensory Components Under the Combined Effect of Vestibular and Visual Stimuli," author abstract of doctoral dissertation, Leningrad, 1977.

7. Kislyakov, V. A., and Levashov, M. M. FIZIOL. ZH. SSSR, No 3, 1971, pp 380-392.

8. Kurashvili, A. Ye., and Babiyak, V. I. "Physiological Functions of the Vestibular System," Leningrad, 1975.

9. Levashov, M. M. ZH. USHN., NOS. I GORL. BOL. [Journal of Ear, Nose and Throat Disease], No 2, 1978, pp 8-13.

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UPGRADING EFFICACY OF MEMBRANE TECHNIQUES FOR REGENERATING WATER FROM URINE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1980 pp 82-83

[Article by B. A. Adamovich, V. D. Volgin, N. M. Nazarov, Yu. Ye. Sinyak and S. V. Chizhov, submitted 3 May 78]

[Text] The most effective of all membrane [diaphragm] methods of regenerating water from urine are those involving evaporation through membranes and back osmosis. Since urine is an aqueous solution, most constituents of which are not volatile or minimally so, evaporation through a membrane, which is not semipermeable, yields water of a good quality that only requires some additional treatment. In this case, polymer film or porous diaphragms made of, for example, cermet [metal ceramic].

Since semipermeable membranes based on acetate cellulose retain up to 99% sodium chloride, while polyamide membrane retain up to 80-90% urea, there was a real possibility of developing a competitive system of regenerating water from urine on the basis of reverse [back] osmosis.

Any membrane consists of a porous diaphragm [wall, barrier], on the surface of which the process of separation of water from other urine components takes place. The concentration of these components increases (concentration polarization), and if they are slowly diverted from the interface a sediment is formed. This sediment accumulates on the membrane surface and is deposited in its pores, which leads to rapid decrease, not only in rate of the process but in selectivity of separation of the solution. For example, in a device where urine is evaporated through porous cermet plates 0.15 mm in thickness with mean pore size of 2 μm, output decreased by more than 4 times in 20 days of continuous operation. However, formation of a sediment did not affect the quality of the obtained water: biochromate oxidizability constituted 100 mg O_2/ℓ, permanganate oxidizability 9.75 mg O_2/ℓ, ammonia content was 8.52 mg/ℓ, odor was rated at 5 points and transparency 30 cm. In the case of back osmosis, there was the same decline in output, which was associated with gradual increase in stained layer of sediment containing urea and sodium chloride on the filter.

Thus, one of the main prerequisites for improving the efficiency of membrane devices amounted to taking steps precluding formation of a sediment. This can be achieved only if a solution containing components in amounts far from saturation is delivered to the apparatus. Since urine is a virtually saturated solution with respect to many constituents and left to stand there often spontaneous precipitation of sediment, one of the mandatory steps is to lower the concentration of urine components. The possibility was considered of partial isolation of the sediment from urine by cooling it and altering the pH. According to the results of 6 tests, cooling urine to 5°C led to precipitation of 4.83±0.95 g/ℓ sediment, while a change in pH to 10.0 led to formation of 10.6±0.8 g/ℓ sediment.

Thus, cooling and alkalinization made it possible to decrease by almost 40% the overall concentration of urine constituents.

Since two-stage processing is technically more complicated and does not rule out the possibility of decomposition of urea, it was expedient to limit ourselves thereafter to one stage, cooling.

In both cases, the permissible coefficient of extraction was in the range of 65-90%. Moreover, the urine concentrate obtained after extracting 50% water from it and submitting it to the same cooling, enabled us to extract another 85-90% of water without precipitations.

In view of the fluctuations in composition of urine, these figures may be lower in some cases. For this reason, it is recommended to use an extraction coefficient of no more than 50%. In this case, it is expedient to run the regeneration process in 2 stages: primary extraction of up to 50% of the water and secondary extraction of water up to 50% from the urine concentrate, as a result of which total extraction will constitute 75%. The effectiveness of such treatment was tested on a laboratory unit with an evaporator made of porous cermet.

Urine was stored in the refrigerator for 24 h, after which the formed sediment was filtered out on a viscose-chlorine filter. The filtered urine was decanted into the unit and we ran the separation process holding the water extraction coefficient at close to 50%.

For the first 4 days, the productivity of the unit dropped to about one-half, which could be related to stabilization of membrane properties. At the second stage, which lasted 16 days, output remained constant. The overall coefficient of water extraction constituted 74%.

Thus, as a result of this experiment, it was established that one can keep productivity of the unit stable for a long period of time. Analogous results were obtained when water was regenerated by the method of back osmosis. Here, the limiting factor was obstruction of membranes by the sediment, which formed as a result of corrosion of equipment elements and microbial contamination of unpreserved urine.

The difficulty involved in selecting a preservative for urine, as related to physicochemical regeneration systems, lies in the fact that the preservative must stabilize urine composition and bind into a complex volatile and usually highly toxic substances, in addition to a decontaminating action. The preservative must be nontoxic, and its phase (solid, liquid, gas) must be determined by the method used to process urine. In addition, the preservative must not lose its antibacterial properties upon contact with the materials of the system and cause corrosion of the latter. It is also undesirable for a sediment to form from the preservative proper.

Urine can be decontaminated by physical, biological and chemical methods, or combinations thereof. Physical methods include heat and ultrasound, ultraviolet radiation, ionizing radiation and exposure to magnetic fields. However, these physical methods all have a common flaw: they do not have an aftereffect on microflora. Thus far no biological method has been developed for preservation that would be based on antagonism of microorganisms. The chemical method of preserving liquid waste best meets the above requirements. Putman [1] recommends the use of a mixture of sulfuric acid, chromium trioxide and copper sulfate as a urine preservative. Sulfuric acid changes ammonia salts of urine into stable compounds, precluding access of ammonia into regenerated water. At the same time, as a preservative the acid could cause formation of new compounds as a result of dissociation of complex and, first of all, nitrogen-containing, components of urine, which worsen the chemical parameters of regenerated water. We shall list here some of the parameters of quality of water regenerated from urine by the distillation method as a function of its reactivity. The most important parameters of quality of regenerated water are the amount of ammonia nitrogen and bichromate oxidizability. Bichromate oxidizability of regenerated water decreases from 6.0 to 5.0 with decrease in pH of initial urine, and it is lowest at urine pH in the range of 5.0 to 3.0. At urine pH of less than 3.0 the oxidizability of recovered water increases sharply. The findings are different with regard to ammonia content of regenerated water: decrease in amount thereof with decrease in pH of initial urine and increase with increase in pH. Urine pH in the range of 3.0 to 5.0 is the optimum for recovering the best quality of water; however, at urine pH of 4.0-5.0 conditions develop that favor development of lower fungi. When the pH is lowered to 3.0, a decontaminating effect lasting up to 3 months is obtained. In the absence or inadequate efficacy of preservative, the water regenerated from urine will have bichromate oxidizability of several hundred milligrams oxygen per liter, and ammonia nitrogen up to several thousand milligrams per liter. Such water requires substantial additional treatment.

Thus, membrane separation methods can be used with success to regenerate water from urine after reliable methods are developed for preserving urine and removing mechanical and colloid impurities from it.

BIBLIOGRAPHY

1. Putnam, D. F. "Paper Am. Soc. Mech. Eng.," NAW-24, 1965, p 13.

UDC: 612.216-087

USE OF POLYURETHANE FOAM DEFORMATION SENSOR TO RECORD RESPIRATORY ACTIVITY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1980 pp 84-85

[Article by V. I. Bredov and V. S. Baranov, submitted 20 Feb 79]

[Text] Various types of sensors are used to record respiratory activity. Special requirements are made of such devices in the case of biotelemetry studies: they must be small in size and weight, reliable, simple in construction, convenient to use, etc.

The sensor developed by V. S. Baranov [1] has some substantial advantages over other known types [2, 3]. It is highly sensitive over a wide range of strain loads. The level of the output signal is linearly related to the force exerted on it, and it is sufficient for direct recording without using amplifiers of electric signals. The sensor is based on elastic, spongy material, polyurethane foam (porolon) with current-conducting material on the pore surface, current-conducting carbon black or electrode paste. In the latter case, the sensitivity of the sensor is somewhat greater. The elastic properties of the sensor are built in the actual base of the strain-sensitive element, which simplifies the construction substantially and increases the reliability of the unit.

Figure 1 illustrates the ohmic resistance of the strain-sensitive element as a function of magnitude of applied load.

In order to test the possibility of using this sensor to examine respiratory function, we recorded human pneumograms with the subject in a calm state. Figure 2 illustrates the tracing of the respiratory curve. We also recorded respiratory activity of experimental animals (dogs). Figure 3 illustrates samples of such tracings.

The simplicity of design of the sensor makes it possible to use it in various physiological experiments, when the parameter measures is related to mechanical loads or can be transformed into them, for example when recording motor activity in actography, taking respiration tracings during submersion under water or ascent to high altitudes.

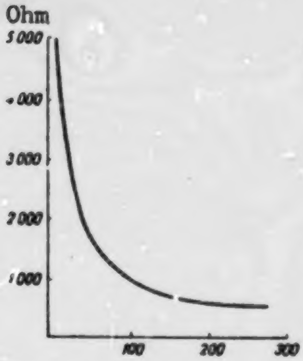

Figure 1.
Change in ohmic resistance of a sample of strain-sensitive element as a function of applied force. X-axis, load (g); y-axis, resistance (in ohms)

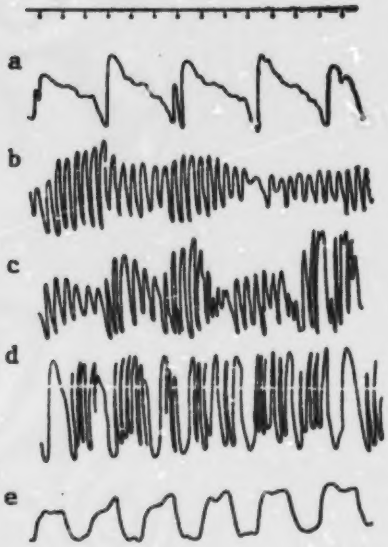

Figure 3.
Pneumogram of experimental animal in the presence of different functional states

a) standing, calm state
b) with delivery of conditioned sonic stimulus
c) during movement (depressing pedal with paw) during exposure to conditioned sonic stimulus
d) pain stress (electrodermal stimulation)
e) experimental neurosis.

X-axis, time (1-s graduation)

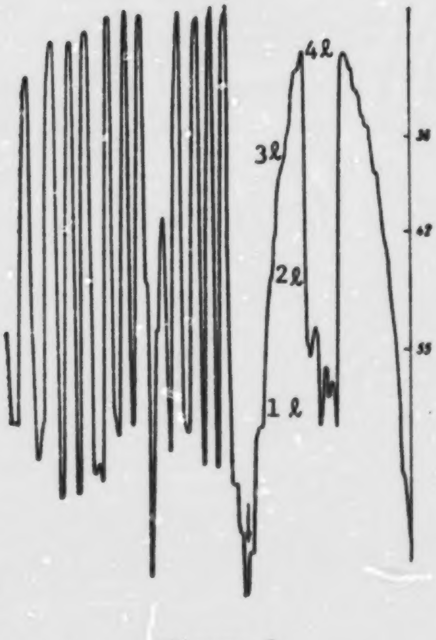

Figure 2.
Human pneumogram with individual in a calm state, standing. The arrow shows deep expiration and the numbers refer to measured inspiration

BIBLIOGRAPHY

1. Baranov, V. S. "Author Certificate 507770 (USSR)," OTKRYTIYA [Discoveries], No 11, 1976.

2. Bayevskiy, R. M. "Physiological Methods in Cosmonautics," Moscow, 1965, p 215.

3. Karnaukhova, N. A. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1974, p 82.

BRIEF REPORTS

UDC: 612.273.2+612.014.477-063].017.2

INFLUENCE OF SPECIFIC CONDITIONING ON WHITE RAT RESISTANCE TO THE COMBINED EFFECT OF HYPOXIA AND -G ACCELERATIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 85-86

[Article by M. A. Kolesov, submitted 28 Jun 77]

[Text] Our objective here was to make a comparative study of the efficacy of specific conditioning methods for the purpose of enhancing resistance to the combined effect of hypoxic hypoxia and negative accelerations.

Methods

The studies were conducted on 183 male mongrel white rats weighing 180-240 g. The animals were divided into five groups. The first consisted of rats rotated once on a centrifuge (65 cm arm), placed in a PBK-53 pressure chamber 5.6 m^3 in size, at an "altitude" of 6500-7250 m, without prior conditioning. The rotation generated accelerations of 2.4 units in the pelvis-head direction lasting 48 min. The second group of rats was submitted to accelerations under the same conditions in a head-pelvis direction; the third group of animals underwent daily conditioning for hypoxia for 1-3 months in the pressure chamber prior to rotation at accelerations of 2.4 units in the pelvis-head direction at high "altitude." Conditioning began with initial "ascent" to 4000 m, then the "altitude" was gradually increased and reached 8000-9000 m at the end of the training period. The rate of ascent and descent constituted 30 m/s. The time the animals spent in the chamber increased from 1 to 4 h. The fourth group of rats was exposed repeatedly (at intervals of 1-2 days) to the combined effect of accelerations and hypoxia over a period of 35-40 days. Here, the "altitude" was gradually increased from 3500 m at the start of the experiment to 6000-7000 m at the end, while rotation time increased from 5 to 45-50 min. In the fifth group, the rats were rotated on the centrifuge for 1 h daily for 3 weeks under ordinary atmospheric conditions. The fourth and fifth groups were rotated in accelerations of 2.4 units in the pelvis-head direction. During rotation, the rats were kept in separate box-cages.

Upon conclusion of conditioning, the animals of the third, fourth and fifth groups, like those of the first group, were rotated once at a high "altitude." Animal survival served as a criterion of endurance. In the rats that survived after the experiments and in 20 intact animals we determined organic blood filling. Immediately after the tests, the rats were sacrificed by rapid immersion in liquid nitrogen. We took 100-mg samples of organs (brain, heart, lung, liver, kidney, spleen, femoral rectus muscle) and homogenized them in 8 mℓ 0.007 M aqueous ammonia solution, in which all of the blood hemoglobin changed to oxyhemoglobin. We diluted 0.04 mℓ whole blood in the same amount of the same solution. The homogenates were centrifuged in a TsVR-1 centrifuge at 18,000 r/min for 20 min, after which the clear solution was decanted into a cuvette 1 cm in diameter, then determined extinction at wavelengths of 580, 605 and 630 nm using an SF-14 spectrophotometer [11]. We assayed blood (in mℓ/100 mg tissue) using the following formula:

$$\frac{[E_{580} - E_{605}] - [E_{605} - E_{630}]}{E_{580} - E_{605}} \cdot 0.04,$$

where the dividend is extinction of tissue and divider is extinction of blood. The results were submitted to statistical processing with the use of Student's criterion.

Results and Discussion

The results of the experiments revealed that only 10 (22.8%) out of the 44 rats in the first group survived after single rotation at an "altitude" of 6500-7250 m for 38 min; all 15 rats of the second group, rotated in the head-pelvis direction, survived; 14 (46.6%) out of 30 animals conditioned for hypoxia survived; 21 (61.7%) out of the 34 rats in the fourth group survived and 27 (77.1%) out of 35 survived in the fifth group.

There was increased filling of the brain with blood in all groups. The maximum increase was demonstrated in unconditioned animals rotated in the pelvis-head direction (by 39%). In the conditioned rats of the fourth and fifth groups, there was appreciably less delivery of blood to the brain (by 22%) than in unconditioned ones.

The changes in filling of kidneys were similar. They were not in contradiction to the findings of other authors [1, 2], who observed a decrease in renal blood flow with separate exposure to acute hypoxia and accelerations. Statistically reliable increase in blood flow in the spleen was observed only in rats submitted to pelvis-head accelerations. It may be assumed that plethora of the spleen was in the nature of a reflex and related to some stasis of blood in the pulmonary circulatory system.

It can be concluded on the basis of these data that not only hypoxic, but circulatory hypoxia, which worsened even more delivery of oxygen to the brain [3] as a result of impairment of cerebral hemodynamics and limited endurance of accelerations, were the cause of animal deaths after rotation in the pelvis-head direction.

The obtained data show that it is possible, in principle, to search for effective methods of specific conditioning to enhance resistance to the combined effect of acute hypoxia and gravitational accelerations.

BIBLIOGRAPHY

1. Barkayev, V. V., and Ovsyannikova, G. L. UROL. I NEFROL. [Urology and Nephrology], No 2, 1967, p 3.

2. Pankova, A. S., and Savina, Ye. A. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1973, p 8.

3. Kovalenko, Ye. A., and Chernyakov I. N. "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 21, 1972.

DISCUSSIONS

UDC: 612.821-057:656.7-051

DISTINCTIVE FEATURES OF CHANGES IN PSYCHOPHYSIOLOGICAL PARAMETERS OF CREWS OF CIVIL AVIATION HELICOPTERS AS RELATED TO WORK LOAD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 86-89

[Article by Yu. N. Kamenskiy, submitted 1 Aug 78]

[Text] The wide use of helicopters in the national economy makes it increasingly important to use a scientifically substantiated and differentiated approach to setting standards with regard to work load for their crews. This involves, first of all, a study of the question of fatigability and efficiency of pilots as related to the intensity of the work [flight] load and effect on crew members of adverse flight factors [1-3]. Studies pursued by a number of authors [4, 5] have made it possible to substantiate flight load standards separately for helicopters with one and two pilots aboard. However, this did not take into consideration a number of other factors. Experience in operating helicopters has shown that one must take into consideration, in setting flight load standards, the influence on pilots of such factors as the industrial environment (noise, fibration, uncomfortable temperatures), location of base (main base, operational center, expedition) time of year and climate.

Heretofore, these questions were not covered in any detail in studies dealing with physiology of flying work in the Civil Aviation.

Methods

We observed the crews of Mi-4 (first series) and Mi-6 (second series) helicopters. The first series of observations was conducted in May at ambient temperatures of 18-25°C and the second in the northern regions of European USSR in April, at atmospheric temperatures of 2 to -15°C.

The crew members were examined 30-40 min before and 30-40 min after terminating flights. In all, we examined 20 members of Mi-4 helicopter crews and 66 of Mi-6 helicopter crews. The crew members of the Mi-4 helicopters made flights daily over the entire work week. The examinations before and after flights were also made daily. The crews of Mi-6 helicopters worked at 1-2-day intervals during the week, with 3 to 7 h flying time daily. The crew members of the Mi-6 helicopters were divided into three groups according to daily flying time: the first group consisted of personnel with daily flying time of up to 5 h (24 people), the second with up to 6 h flying time (22 people) and the third, up to 7 h (20 people).

We studied the following parameters: critical fusion frequency (CFF), static tremorometry (ST), reaction to a moving object (RMO) and reproduction of a specified muscular exertion (RME). We studied the subjective evaluation by pilots of working conditions by means of anonymous questionnaires. The results were processed statistically using the criteria of Student.

Results and Discussion

In the pilots of Mi-4 helicopters, the base values of psychophysiological parameters changed inconsistently from day to day. Conversely, the postflight changes presented distinct weekly dynamics (Figure 1). After the first work day, there was a reliable increase in ST (by 79±9%) and percentage of RME deviations (by 88±20), as well as accuracy of RMO (by 54±12%). After the second and third work day, the postflight changes were considerably less marked. After completing the flights on the 4th day, we observed a reliable increase in ST and RME (by 78±10 and 150±14% of the base levels, respectively). On the 5th and 6th days, there was a reliable decrease in CFF (by 12±2 and 13±4%, of base values, respectively) and accuracy of RMO (by 56±9 and 52±7%). Thus, the dynamics of postflight changes in psychophysiological parameters were characterized by marked changes after the 1st flight day, decreased changes and relative stabilization after the 2d and 3d days, and a gradual second increase starting on the 4th day. The severity of changes in the parameters studied on the 1st and 6th days corresponded to grade III fatigue according to Ye. F. Polezhayev and V. A. Yepikhin [6].

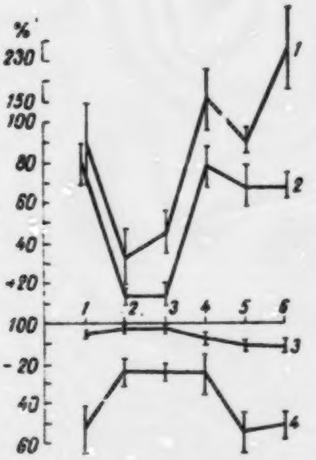

Figure 1.
Dynamics of changes in psychophysiological parameters of Mi-4 pilots in the course of a work week. X-axis, work days; y-axis, changes in parameters as related to initial levels.

Consequently, there was phasic change in functional state of the Mi-4 pilots during the work week: The first phase corresponded to the 1st day of work and was characterized by development of marked fatigue, which could be the result of partial deconditioning for the work loads and working conditions during the preceding time off. The second phase, which coincided with the 2d and 3d work days, could be indicative of adaptation of the pilots to the work loads. If we use adaptation to refer to an increase in physiological capabilities and increase in performance [efficiency] [7], apparently there was the highest level of safety of flights during this period because of the human [personal] factor. The third phase began on the 4th day of flights, and it can be qualified as a manifestation of depletion of functional reserves, which could lead to diminished performance.

For expressly this reason, one should not recommend daily flights on helicopters for 6 consecutive days with daily flying time of 7 h. It is necessary to use a somewhat altered flight schedule. One of the variants could be to have flights for 3-4 days followed by 1-2 days of rest. Another variant could be based on the same schedule, but decreasing flying time on the 1st day after time off by 1-2 h.

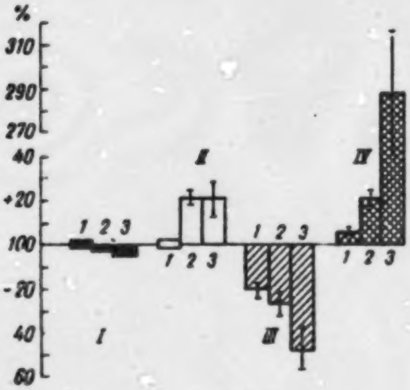

Figure 2.
Changes in psychophysiological parameters of Mi-6 pilots as related to different daily flying times

I) CFF
II) ST
III) RMO
IV) RME

1) 5 h flying time
2) 6 h
3) 7 h

Analysis of the results of the second series of studies revealed that the changes in psychological parameters were insignificant in Mi-6 pilots flying up to 5 h per day. With up to 6 h flying time, reliable changes in parameters were demonstrated, as compared to both base levels and postflight findings in the first group: 27±4% decrease in accuracy of RMO, 20±3% increase in RME error, while ST increased by 21±3% (Figure 2). The most substantial changes were noted in crew members who flew up to 7 h per day: RMO accuracy decreased by 50±9%, RME error increased by 290±28% and ST index increased by 21±8% (see Figure 2). With flying time of up to 5 h daily, the functional state of crew members corresponded to grades I-II fatigue according to the classification of Ye. F. Polezhayev and V. A. Yepikhin; it was rated as grade II with up to 6 h flying time and characterized by early signs of fatigue, and as grade III with flying time of up to 7 h, which was characterized by marked fatigue.

Of course, development of fatigue was associated with diminished performance. Under ordinary flying conditions, this does not necessarily have a substantial effect on quality of decision making and piloting, but when flying conditions are more complex (poor visibility, snow, "bumpy" air, technical malfunction) there could be preconditions for flight incidents. Instances of loss of spatial and geographic orientation by pilots, appearance of spatial illusions in difficult situations have been described [8-10].

It is known that pilots develop fatigue not only under the influence of flight work, but exposure to concomitant factors, particularly vibration and noise [1, 5, 11-13]. The vibration and noise levels may reach high intensities in the crew's cabins of modern helicopters [14-16]. This warrants the assumption that vibration and noise did not play the last role in development of fatigue among the crew members of Mi-4 and Mi-6 helicopters. Special mention should be made of the possible influence of vibration, as confirmed by the drastic changes in accuracy of RME with flying time of 6 h or more. The RME is probably the most adequate of the set of parameters used with respect to vibration, since the afferent element of the arc of this reflex begins at the mechanoreceptors of the motor analyzer. At the same time, the findings of a number of studies suggest that vibration is a specific stimulus for mechanoreceptors [17-19].

The assumption that vibration plays a significant role in development of fatigue is also confirmed by the results of analysis of subjective data. All of the pilots rated vibration and noise as the most unpleasant factors. Vibration was rated even worse than noise (30.7% of the answers); noise was more unpleasant than vibration for only 10.5% of those questioned; noise and vibration were equally unpleasant for 58.8%.

Fatigue is the natural result of any work. The question is only of the degree of fatigue. If we were to assess the postflight changes from this position among the crew of Mi-6 helicopters involving different daily flying times, a 6-h/day standard can be considered warranted. The question of a 7-h daily flying time can be answered in the affirmative provided there is further improvement of work schedule for helicopter crews and decrease in their exposure to deleterious flight factors, first of all vibration and noise.

Thus, there must be differentiated determination of work standards aboard helicopters of the Civil Aviation and it must take into consideration working conditions (noise, vibration, other adverse flight factors). Differentiated and scientifically substantiated standards for flying time aboard helicopters will reduce pilot fatigue and provide for a high performance, which will be instrumental in further increase in safety of flights.

BIBLIOGRAPHY

1. Gurovskiy, N. N. GIG. I SAN. [Hygiene and Sanitation], No 3, 1959, pp 27-33.

2. Kuleshov, V. I. VOYEN.-MED. ZH. [Military Medical Journal], No 2, 1977, pp 60-62.

3. Billings, Ch. E.; Gierke, R. J.; Chase, R. C.; et al. AEROSPACE MED., Vol 44, 1973, pp 1026-1030.

4. Mirzoyev, B. M.; Ostrovskiy, V. F.; Loktev, I. V.; et al. in "Kosmicheskaya biologiya i aviakosmicheskaya meditsina" [Space Biology and Aerospace Medicine], Moscow--Kaluga, Vol 2, 1972, pp 126-129.

5. Ustinova, A. I.; Ostrovskiy, V. F.; Onufrash, A. I.; et al. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, Vol 1, 1975, pp 124-127.

6. Polezhayev, Ye. F., and Yepikhin, V. A. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1976, pp 83-84.

7. Frolov, V. M. "Functional Levels of Physiological Systems and Methods for Determination Thereof," Leningrad, 1972.

8. Malov, Yu. S. VOYEN.-MED. ZH., No 9, 1964, pp 58-62.

9. Graybiel, A., and Clarke, K. B. J. AVIAT. MED. Vol 16, 1945, pp 111-151.

10. Simson, L. R. AEROSPACE MED., Vol 42, 1971, pp 1002-1005.

11. Kulikovskiy, G. G. in "Osnovy aviatsionnoy meditsiny" [Fundamentals of Aviation Medicine], Moscow--Leningrad, 1939, pp 119-128.

12. Noseliani, K. K. KOSMICHESKAYA BIOL., No 2, 1967, pp 79-82.

13. Molchanov, N. S.; Sil'vestrov, V. P.; Chireikin, L. V.; et al. in "Kosmicheskaya biologiya i aviakosmicheskaya meditsina," Moscow--Kaluga, Vol 2, 1972, pp 36-38.

14. Borshchevskiy, I. Ya.; Koreshkov, A. A.; Markaryan, S. S.; et al. VOYEN.-MED. ZH., No 1, 1958, pp 74-77.

15. Gabel, R.; Henderson, B. O.; and Reed, D. A. J. AM. HELICOPT. SOC., Vol 16, 1971, pp 39-43.

16. Weiland, E. F. Ibid, Vol 14, 1969, p 22.

17. Andreyeva-Galanina, Ye. Ts. "Vibration and Its Significance in Industrial Hygiene," Leningrad, 1956.

18. Egger, M. REV. NEUROL., Vol 10, 1904, p 549.

19. Ernsthausen, W. in "German Aviation Medicine World War II," Washington, Vol 2, 1950, pp 651-685.

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Vol. 14, No. 3, 1980

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Vol. 14, No. 3, 1980

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BIOCHEMICAL BASES OF PATHOGENESIS OF HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 3-10

[Article by I. V. Fedorov, submitted 18 Sep 78]

[English abstract from source]

The paper describes an attempt to gain an insight into pathogenetic mechanisms and sequence of reactions responsible for changes in the metabolism of proteins, carbohydrates and fats of hypokinetic animals.

[Text] Hypokinesia has a dual effect on the body. There is decrease and change in flow of afferent and, consequently, efferent impulsation, and the body is deprived of their constant regulatory influence. The abrupt change from a state of movement and work to immobilization and rest acts as a stressor, and the greater the difference between these two states the stronger it is.

Direct and indirect evidence has been accumulated to date of the fact that there is decreased intensity of synthesis of tissular proteins and increased intensity of their breakdown in hypokinetic animals and man [1-6].

What are the mechanisms of change in protein metabolism of hypokinetic animals?

Protein synthesis is the unity of three flows: of energy, matter and information. Information about synthesis of individual proteins is contained in the appropriate structural genes, sections of the DNA molecule. According to our conceptions, blocking of the flow of information is the primary and decisive factor in lowering synthetic processes in the presence of hypokinesia.

According to total assays [7] by the method of Schmidt and Thannhauser in the modification of Tsanev and Markov, absolute DNA content of all tissues (with the exception of muscle) of hypokinetic animals did not change appreciably, whereas in muscle tissue it increased significantly.

We consider this to be a relative increase, occurring as a result of dissociation of myofibrillar and sarcoplasmic proteins, with preservation of nuclear material rich in DNA. As we see, no shortage of the substrate of information is demonstrable. RNA content of tissues, which was assayed by the same method, did not change or even increased. Most of the cellular RNA (over 80%) consists of ribosomal RNA (rRNA). But we are concerned mainly with messenger RNA (mRNA), the level of which did not exceed 2%. It is difficult to judge the changes in mRNA alone when assaying the sum of all cellular RNA.

The flow of information is limited primarily by the intensity of the transcription process. Afferent signals going to the central nervous system from functional muscles stimulate neural trophics, including the autonomic nervous system, which has an adaptive-trophic effect on all tissues, including skeletal muscles [8, 9]. It has been shown that an increase in gene activity, as manifested by increased activity of DNA-dependent RNA polymerase, i.e., intensity of the transcription process [10], is the basis of muscular adaptation to regular muscular exercise.

It is to be assumed that, in the presence of hypokinesia when there is significant attenuation and distortion [11] of afferent impulsation, there is a decrease in gene activity, since no derepression of structural genes occurs, which normally takes place under the influence of constant impulses from numerous interoceptors of functional muscles. Unfortunately, no determination was made of gene activity in hypokinetic animals. However, there are a number of facts serving as indirect proof of the validity of such hypotheses. Thus, giving immobilized animals a balanced (mainly protein) diet and anabolic hormones does not lead to restoration of protein synthesis in skeletal muscles. These processes start to recover only when the animals resume motor activity.

Hypokinesia, particularly during the first few weeks, acts like an unusual stress stimulus, which is confirmed by increased production of epinephrine, increased ACTH content of blood plasma [12-15], an increase in weight of the adrenals, hypertrophy of their cortex with proliferation of the fascicular layer, increased synthesis and secretion of corticosteroids [15-17]. The statistically reliable decrease in eosinophils of peripheral blood is also indicative of increased secretory activity of the adrenal cortex. At later stages of hypokinesia (over 60 days), there is development of depletion of the system of the hypothalamus-hypophysis-adrenal cortex, with corresponding decrease in adaptational capabilities of the organism.

Depression of synthetic and processes and activation of catabolic processes in most tissues is inherent in stress reactions, particularly in skeletal muscles, as was manifested in hypokinetic animals.

The influence on protein synthesis of changes in the other two flows (of matter and energy) is unquestionable, although it is not decisive.

Amino acids for protein synthesis arrive with feed proteins. During the first week of hypokinesia there is some decrease in feed intake; however, it then holds at the same level as in healthy animals [4, 18]. In the 2d-3d week of hypokinesia, total free amino acids in tissues, including muscle, increase by 10%, but there is a change in proportion of different amino acids [19].

With prolonged (60 days) hypokinesia, total amino acid content drops by almost 20%, mainly referable to unessential amino acids. This is related to increased excretion of amino acids in urine, use thereof to detoxify toxic products and as energy material. The shortage and imbalance of amino acids have an adverse effect on protein synthesis; however, most probably the change in information from structural genes is the primary cause of uneven utilization thereof in tissues: increased uptake of some and output of others. Then, the reaction apparently develops on the order of a vicious circle, as a result of which there is an even greater shortage and imbalance of some amino acids. The failure to normalize nitrogen equilibrium in hypokinetic humans by means of diet alone confirms our hypothesis. It is not such much a matter of shortage of material for protein synthesis as the impossibility of utilizing this material.

Potassium is one of the elements necessary for protein synthesis [20, 21]. On the 12th, 22d and 30th days of hypokinesia, the level thereof in rat muscles decreased by 12, 3 and 5%, respectively, of the control level [11, 22]. A substantial decrease is observed in potassium concentration in rabbit muslces 1 month after the start of hypokinesia [23]. In hypokinetic humans, there is increased excretion of potassium in urine.

The potassium deficiency can have an adverse effect on protein synthesis under hypokinetic conditions.

Protein synthesis requires energy. However, under hypokinetic conditions, metabolism of carbohydrates and lipids, oxidation of which produces most of the body's energy, is appreciably affected. The macroerg deficiency may be one of the causes of depression of synthetic processes.

Intensification of protein catabolism was manifested by increased excretion of products of their breakdown, negative nitrogen balance and decrease in absolute protein content of tissues.

As we see it, such a reaction is attributable to at least three causes. At the first stage (1st-3d weeks), hypokinesia acts like an unusual stress stimulus. The general response to any stressor is development of the catabolic phase of the general metabolic reaction. First of all, the process involves skeletal muscles, the products of breakdown of which are eliminated from the body and partially used as plastic material to maintain synthetic processes in vital organs. With increase in glucocorticoid production, there is stimulation of gluconeogenesis due to activation of tissue proteases and aminotransferases which are instrumental in protein breakdown [5, 24, 25].

It is known that when some part of the body is immobilized the components of its tissues are gradually destroyed. Thus, atrophy of extremital muscles is observed with the prolonged presence of a plaster cast, traumatic and surgical denervation, and tenotomy. This is so-called disuse atrophy. In the presence of hypokinesia, there is forced disuse of many muscle groups. It is not surprising then that proteins and other components of skeletal muscles begin to break down. This applies, first of all, to functionally active proteins, myofibrils and sarcoplasm. Cuthberson [26] made a study of sulfur and total nitrogen of urine in humans submitted to prolonged hypokinesia. He established that there is significant increase in elimination thereof, but the proportion between them remains the same as in proteins of skeletal muscles, which is indicative of predominant breakdown of the latter under hypokinetic conditions. One can also refer to partial destruction of skeletal muscles on the basis of tests on assimilation of creatine. It is known that creatine is assimilated by skeletal muscles. It was given with food. Before hypokinesia, over 80% of the creatine was assimilated and during hypokinesia assimilation decreased by 11-70%.

The third cause is as follows. The fact of the matter is that nitrogen, sulfur and phosphorus are excreted in urine in high quantities because considerably less of them can be utilized for synthetic processes.

In skeletal muscles, there is a decrease in share of myofibrillar and sarcoplasmic proteins and a corresponding increase in relative amounts of stromal proteins, proteins of fraction T [27, 28]. There is a significant increase in collagen content of skeletal muscles and the heart [29]. It should be assumed that these changes can have an adverse effect on functional capacity of muscles, particularly in the rehabilitation period following prolonged hypokinesia.

Carbohydrate metabolism undergoes a number of changes in hypokinetic animals. One of the typical ones is a decrease in glycogen content. Tissues became poor in the main substrate of respiration, glycogen [30, 33].

There was a change in blood sugar level concurrently with change in glycogen content.

Oxidation of carbohydrates was impaired. First, the aerobic route of their conversion was impaired. P/O coefficient decreased by 2-5 times, and there was dissociation of processes of respiration and phosphorylation [34-36]. Carbohydrate metabolism changed to energetically less advantageous anaerobic oxidation--glycolysis and glycogenolysis, and the intensity of the last two processes increased [33, 37]. At later stages (2-3 months) there was also depression of anaerobic processes [11, 33, 38].

As mentioned above, impairment of carbohydrate-energy metabolism affects protein synthesis and unquestionably has an adverse effect on conversion of other substances.

What are the causes of impairment of carbohydrate metabolism? Mobilization of carbohydrate resources by means of dissociation of glycogen in skeletal muscles and the liver is one of the usual manifestations of a stress reaction. Breakdown of glycogen is stimulated by increased access of epinephrine. Then, with increase in production of glucocorticoids, which activate the enzymes of gluconeogenesis and glycogen synthetase, there is a rise of glycogen level in the liver and skeletal muscles, as compared to the preceding stage (3d and 15th days), but it does not reach the base levels. There is depletion of protein and lipid resources as material for synthesis of glycogen. There is greater manifestation of glucogen requirement as energy material, since oxidative phosphorylation is depressed and there is prevalence of a less efficient route of macroerg production, glycogenolysis and glycolysis. The liver loses glycogen as a result of detoxification of breakdown products. Since there is accumulation of a large amount of products of protein breakdown in the presence of hypokinesia, detoxification thereof may be one of the causes of decrease in glycogen content of the liver.

Intensive dissociation of glycogen reserve and stimulation of gluconeogenesis cause hyperglycemia, which is inherent in the early stage of hypokinesia. At the later stages, hyperglycemia is replaced by persistent hypoglycemia, since by this time the store of glycogen is depleted, while de novo synthesis is inhibited. Increased sensitivity to insulin may also be involved in development of hypoglycemia [30].

According to I. A. Arshavskiy [39], motor activity is a factor in functional induction of anabolism. The data pertaining to change in glycogen content of skeletal muscles and the heart of hypokinetic animals confirm this. The myocardium functions continuously. By the 30th-60th day of hypokinesia, after initial stress dissociation, the glycogen reserve of the heart is restored almost to base levels due to de novo synthesis. By the 30th-60th days, there was still very little glycogen in skeletal muscles of the femur, which were virtually nonfunctional. The reserve thereof was not replenished under hypokinetic conditions. In the recovery period, however, after returning to the usual motor activity, glycogen content reached the base levels. There was a decline of glycogen level in the liver, as in muscles proper, with inactivity of skeletal muscles, and it was restored when they resumed activity. The main factor in impairment of carbohydrate-energy metabolism is the decreased production of macroergs due to dissociation of oxidation and phosphorylation in the respiratory chain. The intimate mechanisms of ATP production in oxidative phosphorylation have not yet been identified. For this reason, it is difficult to discuss the true causes of change in these processes under the influence of some factor or other, including hypokinesia. We conceive of the following sequence of reactions as a working hypothesis. Hypokinesia, acting like a stress factor, causes increased production of epinephrine [12-15]. Epinephrine activates lipases of fatty tissue and stimulates an increase in concentration of nonesterified fatty acids (NEFA) in tissues. Indeed, in hypokinetic rats there is appreciable increase in lipase activity of fatty tissue and 1.5-2-fold increase in NEFA concentration. Free fatty acids are one of the factors of dissociation of oxidative phosphorylation [40] and increased mitochondrial permeability to other oxidation substrates. Both of these factors lead to a decline of P/0 ratio. Moreover, utilization of NEFA as an oxidation substrate lowers P/0 even more, since this involves elimination of one of the links of conjugation, due to formation of $NADP \cdot H_2$, rather than $NAD \cdot H_2$, at the first stage of β-oxidation.

In nonfunctioning muscles, there is no need to split ATP as a source of energy for muscular contraction. If there is no splitting of ATP there is no formation of ADP. The latter is a stimulator of oxygen uptake and formation of new ATP molecules in the course of oxidative phosphorylation.

With intensification of proteolysis, there is formation of superfluous ammonia, which binds oxalacetic and α-ketoglutaric acids, the main components of the tricarboxylic acid cycle (TCC). As a result, there can be a decrease in passage of reduced coenzymes from the TCC into the respiratory chain [41].

Energy of the respiratory chain is not used for ADP phosphorylation, but for active transport of substance and production of heat [38, 42].

With impairment of phosphorylation in the respiratory chain as the main supplier of macroergs, an emergency mechanism of energy supply is triggered, i.e., glycolysis [43]. In view of partial dissociation of respiration and phosphorylation, these processes can no longer successfully compete with glycolysis for ADP and phosphate. Expressly such a situation develops in the presence of hypokinesia. During the first weeks of hypokinesia, there is intensification of glycolysis and glycogenolysis in animals. There has been demonstration of stimulation of glycolysis in skeletal muscles of hypokinetic rats [44, 45]. This is also indicated by the numerous data pertaining to accumulation of lactic acid and some decrease in pyruvic acid in blood and tissues [6, 32, 33, 38]. Intensification of glycolytic processes compensates for the shortage of macroergs for only a brief time. Under hypokinetic conditions, there is considerable limitation of reserves of glycogen due to intensified breakdown and decreased synthesis thereof. Glycolysis and glycogenolysis become energetically less efficient, and for the production of the required amount of ATP considerably more substrates are used, which causes even greater depletion of the already sparse reserves. After 2-3 months, the shortage of carbohydrates and decreased activity of some glycogenolytic enzymes (phosphorylase, aldolase) [43-46] lead to weakening of the anaerobic route of carbohydrate conversion. Inhibition and blocking of glycolysis and the TCC under hypokinetic conditions induce compensatory increase in carbohydrate oxidation in the pentose cycle. Increased production of glucocorticoids, which is typical of hypokinesia, is also involved in intensifying direct oxidation of carbohydrates. However, the pentose cycle is chiefly a supplier of pentoses and $NADP \cdot H_2$, and to a lesser extent macroergs. They become more intensively involved in lipid metabolism to compensate for the shortage thereof.

A number of changes in lipid metabolism was demonstrated in hypokinetic rats and rabbits [6, 29, 47–49]. In animals (particularly rats) there was a decrease in lipid reserves and substantial decrease in total lipids of tissues. There was an increase in cholesterol content of blood and tissues of rat skeletal muscles, heart, liver and kidneys. Studies of blood serum lipoproteins of hypokinetic rats by the method of disk electrophoresis on polyacrylamide gel showed an increase in the pre-β-lipoprotein fraction, β-lipoproteins, as well as albumins in a complex with NEFA. The increase in levels of these fractions indicated that, under hypokinetic conditions, there was an increase in endogenous triglycerides (pre-β-lipoproteins), cholesterol (β-lipoproteins) and NEFA in the animals' blood. In rats, there was a 30–45% increase in lipolytic activity of fatty tissue. There was concurrent increase in serum NEFA content, from 50 to 129%. There was a drastic increase in acetone body content (to 470%).

There is much in common between the genesis of disturbances referable to carbohydrate and lipid metabolism under hypokinetic conditions, in view of the close correlation between conversions thereof in the body. Stress caused by hypokinesia induces an increase in production of epinephrine and glucocorticoids. Both hormones are involved in mobilizing lipids from the fat depot. In the presence of hypokinesia, there is substantial increase in fatty tissue lipase activity under the influence of epinephrine and glucocorticoids, which leads to an increase in NEFA content. Intensification of lipolytic activity is one of the causes of depletion of fat depots and decrease in lipids of skeletal muscles and liver, as well as decline of triglyceride levels in many tissues after 15 and 30 days of hypokinesia. Impairment of carbohydrate metabolism is the second cause. As we know, the blood glucose level regulates lipid synthesis and breakdown. In rats, one observes hypoglycemia, decreased intensity of carbohydrate metabolism via the glycolytic and, particularly, oxidative pathways. When there is a glucose deficiency, there is increased breakdown of lipids and inhibition of de novo production thereof. Glycerophosphate is needed for lipogenesis, and it is generated in the course of glycolysis. Under normal conditions, NEFA are metabolized very rapidly, so that the levels thereof are low in serum. Under hypokinetic conditions, conversion of NEFA is slower. This is attributable to several causes. There is faster breakdown of triglycerides than utilization thereof, in particular due to the fact that liposynthesis is inhibited by the shortage of glucose, and there is not enough glycerophosphate. Citrate activates one of the main enzymes of fatty acid synthesis, acetyl-CoA-carboxylase, and there is less access of citrate when the TCC is blocked.

The subsequent fate of fatty acids is oxidation in the β-cycle, with formation of acetyl-CoA. In hypokinetic animals, the reserves of free acetyl-CoA are replenished by means of intensified breakdown of carbohydrates and conversion of glucogenic amino acids, in addition to β-oxidation. An overt surplus of this important substrate is formed. In healthy animals, active acetic acid, which burns up in the TCC, delivering hydrogen to the oxidative chain, is used for synthesis of cholesterol, fatty acids and acetone bodies. As shown above, under hypokinetic conditions there is impairment of oxidation of acetyl-CoA in the TCC, with dissociation of processes of oxidation and phosphorylation in the respiratory chain and inhibition of de novo synthesis of fatty acids. In this situation, synthesis of cholesterol and acetone bodies are the chief means of utilizing active acetic acid. Indeed, a substantial increase in blood and tissue cholesterol content and blood β-lipoprotein content, the main transport form of cholesterol, was observed in hypokinetic animals. The levels were particularly high on the 15th and 90th days of hypokinesia. At expressly these times there was demonstration of maximum increase in enzymes of the pentose cycle- glucose-6-phosphate dehydrogenase and 6-phosphogluconic acid dehydrogenase, which delivers the $NADP \cdot H_2$ product required for cholesterol synthesis. Along with increase in cholesterol content, there was a significant increase in acetone bodies; consequently, part of the accumulated surplus of acetyl-CoA was used to produce them. The carbohydrate deficiency was also involved in this. The cholesterol surplus depresses glycolysis [50] which, in turn, is instrumental in impairment of fat metabolism, with respect to even more production of cholesterol and acetone bodies. The vicious circle closes. Such parameters of carbohydrate and fat metabolism as depletion of glycogen reserve, emptying of fat depots, lipemia and acetonemia are observed in the presence of hypokinesia and diabetes mellitus. It is quite likely that a shortage of insulin is one of the causes of this, as is the case with diabetes. There are no data in the literature concerning insulin levels in hypokinetic animals and man. However, there are grounds to assume that insulin content was relatively low, since there was a substantial increase in production of its antagonists, epinephrine, glucocorticoids and adrenocorticotropic hormones.

These are, in our opinion, the causes of changes in fat metabolism of animals submitted to rigid hypokinetic conditions.

In the presence of hypokinesia, there is a change in composition of many tissues, particularly skeletal muscles, in the direction of sclerosis, replacement of part of the active proteins of sarcoplasm and the actomyosin complex with connective tissue proteins. A quantitative evaluation of these processes was first made by P. P. Potapov [29], who assayed collagen (according to hydroxyproline), total (according to glucosamines) and acid (according to hexuronic acids) mucopolysaccharides.

Collagen content of skeletal muscles increased by 40% on the 15th day of hypokinesia and by 48% on the 60th-90th days, as compared to the control. Hexosamine content decreased by 8.6, 9.4 and 19.6% on the 15th, 30th and 90th days, respectively, while hexuronic acid content reliably increased. By the 60th-90th days, hydroxyproline content also increased in the myocardium and kidneys, and did not change in the liver. At all tested times, there was an appreciable decrease in hexosamine content of the liver, and by the 90th day there was also one in the kidneys. At all times, hexuronic acid content was high in the kidneys, it declined somewhat in the heart and did not change in the liver.

Thus, under hypokinetic conditions there is a significant change in mucopolysaccharide content of many tissues. Fluctuations thereof could play a substantial role in development of disturbances referable to fluid-base equilibrium and tissular permeability; they could be involved in decreasing resistance to infection and affect clotting of blood. As we have already noted, under hypokinetic conditions there is less intensive oxidative phosphorylation, compensatory increase in glycolysis and direct oxidation of glucose. The change to less efficient means of utilizing carbohydrates results in a decrease in resources thereof in the organism. Phosphoric esters of hexoses are the direct precursors of hexosamines and hexuronic acids. One of the chief causes of change in their levels under hypokinetic conditions is a shortage of carbohydrates. The other causes are related to changes in glucocorticoid production and cholesterol content. As we know, adrenocortical hormones depress synthesis of glycosaminoglycans, while cholesterol stimulates production of acid mucopolysaccharides. The increase in connective tissue elements of skeletal muscles can lead to impairment of their function, particularly during the period of readaptation following prolonged hypokinesia. It is possible to make a quantitative evaluation of development of sclerotic processes in skeletal muscles and the heart according to collagen content. A significant increase in the latter, especially at the late stages of hypokinesia, is attributable to an increase in amount of acid mucopolysaccharides, which induce collagen synthesis. On the 60th and 90th days, there is a 42 and 38% increase, respectively in hydroxyproline/hexuronic acid ratio in intramuscular connective tissue. The same direction of changes is inherent in the heart. This is indicative of a shortage of the main substance of connective tissue and its aging.

BIBLIOGRAPHY

1. Fedorov, I. V.; Vinogradov, V. N.; Milov, Yu. I.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 1, 1967, pp 53-57.

2. Fedorov, I. V.; Milov, Yu. I.; and Simonov, Ye. Ye. Ibid, No 3, 1970, pp 18-21.

3. Fedorov, I. V.; Chernyy, A. V.; and Fedorov, A. I. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 8, 1977, pp 1128-1133.

4. Fedorov, I. V., and Grishanina, L. A. KOSMICHESKAYA BIOL., No 3, 1967, pp 43-48.

5. Fedorov, V. I. Ibid, No 5, 1971, pp 82-84.

6. Fedorov, I. V. NAUCH. DOKL. VYSSH. SHKOLY. BIOL. NAUKI [Scientific Reports of Schools of Higher Education. Biological Sciences], No 12, 1972, pp 24-36.

7. Fedorov, I. V., and Shurova, I. F. KOSMICHESKAYA BIOL., No 2, 1973, pp 17-21.

8. Orbeli, L. A. "Selected Works," Moscow-Leningrad, Vol 2, 1962, pp 94, 227, 413, 427.

9. Yakovlev, N. N. "Biochemistry of Sports," Moscow, 1973, pp 53-67, 77-88, 129-136, 205-212.

10. Rogozkin, V. A.; Zil'ber, M. L.; and Pliskin, A. V. VOPR. MED. KHIMII [Problems of Medical Chemistry], No 4, 1974, pp 376-379.

11. Zhukov, Ye. K.; Barbasheva, Z. I.; and Fedorov, V. V. FIZIOL. ZH. SSSR, No 9, 1971, pp 1240-1245.

12. Krupina, T. N.; Mikhaylovskiy, G. P.; and Tizul, A. Ya. in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii" [Adaptation to Muscular Activity and Hypokinesia], Novosibirsk, 1970, pp 94-96.

13. Krupina, T. N.; Tizul, A. Ya.; Baranova, V. P.; et al. Ibid, pp 96-98.

14. Kazaryan, V. A.; Pishchik, V. B.; and Shipov, G. D. Ibid, pp 79-80.

15. Kovalenko, Ye. A.; Mailyan, E. S.; Popkov, V. L.; et al. USPEKHI FIZIOL. NAUK [Advances in Physiological Sciences], Vol 6, 1975, p 3.

16. Kovalenko, Ye. A. KOSMICHESKAYA BIOL., No 1, 1976, pp 3-15.

17. Parin, V. V.; Fedorov, B. M.; and Nevstruyeva, V. S. DOKL. AN SSSR [Reports of the USSR Academy of Sciences], Vol 184, No 1, 1969, pp 250-251.

18. Kovalenko, Ye. A.; Popkov, V. L.; Kondrat'yev, Yu. I.; et al. PAT. FIZIOL. [Pathological Physiology], No 6, 1970, pp 3-8.

19. Fedorov, I. V. KOSMICHESKAYA BIOL., No 5, 1973, pp 35-39.

20. Kovtunyak, N. A., and Meshchishen, I. F. NAUCH. DOKL. VYSSH. SHKOLY. BIOL. NAUKI, No 8, 1971, pp 38-44.

21. Mirskiy, N. P., and Osava, S. in "Funktsional'naya morfologiya kletki" [Functional Morphology of the Cell], Moscow, 1963, pp 9-68.

22. Mikhaleva, N. P.; Ivanov, I. I.; Korovkin, B. F.; et al. in "Eksperimenty issledovaniya gipokinezii, izmenennoy gazovoy sredy, uskoreniy, peregruzok i drugikh faktorov" [Experimental Studies of Hypokinesia, Altered Gas Environment, Accelerations, G Forces and Other Factors], Moscow, 1968, pp 18-21.

23. Krotov, V. P. KOSMICHESKAYA BIOL., No 2, 1972, pp 66-74.

24. Fedorov, I. V.: Milov, Yu. I.; Vinogradov, V. N.; et al. Ibid, No 1, 1968, pp 22-24.

25. Simonov, Ye. Ye., and Fedorov, I. V. Ibid, No 1, 1970, pp 16-18.

26. Cuthberson, D. P. BIOCHEM. J., Vol 23, 1929, pp 1328-1345.

27. Mikhaleva, N. P.; Ivanov, I. I.; Fedorov, I. V.; et al. KOSMICHESKAYA BIOL., No 2, 1970, pp 42-45.

28. Gayevskaya, M. S.; Slez, L. M.; and Ilyushko, N. A. Ibid, No 4, pp 25-29.

29. Potapov, P. O. "Glycosaminoglycans (Mucopolysaccharides), Collagen and Lipids of Tissues in the Presence of Hypodynamia," author abstract of candidatorial dissertation, Moscow, 1978.

30. Chernyy, A. V. KOSMICHESKAYA BIOL., No 1, 1975, pp 23-27.

31. Vinogradov, V. N.; Petrukhin, V. G.; and Fedorov, I. V. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 6, 1968, pp 96-99.

32. Blinder, L. V.; Organov, V. S.; and Potapov, A. N. in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii," Novosibirsk, 1970, pp 37-37.

33. Rassolova, N. P.; Potapova, A. N.; Sapelkina, I. M.; et al. KOSMICHESKAYA BIOL., No 2, 1973, pp 26-33.

34. Ivanova, S. M., and Ushakov, A. S. in "Fiziologicheskiye problemy detrenirovannosti" [Physiological Problems of Deconditioning], Moscow, 1970, pp 118-121.

35. Kovalenko, Ye. A.; Popkov, V. L.; Mailyan, E. S.; et al. KOSMICHESKAYA BIOL., No 4, 1971, pp 3-8.

36. Mailyan, E. S.; Brinberg, L. N.; and Kovalenko, Ye. A. in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii," Novosibirsk, 1970, pp 11-112.

37. Siryk, L. A. BYULL. EKSPER. BIOL., No 10, 1972, pp 22-25.

38. Siryk, L. A., and Tregulov, M. I. Ibid, No 10, 1973, pp 21-24.

39. Arshavskiy, I. A. in "Vedushchiye faktory ontogeneza" [Prime Ontogenetic Factors], Kiev, 1972, p 44.

40. Skulachev, V. P. "Accumulation of Energy in Cells," Moscow, 1969.

41. Gulyy, M. F. "The Main Metabolic Cycles," Kiev, 1968, pp 207-226.

42. Grinberg, L. N. in "Mitokhondrii. Struktura i funktsii v norme i patologii" [Mitochondria: Structure and Functions Under Normal and Pathological Conditions], Moscow, 1971, pp 145-150.

43. Ivanov, I. I.; Korovkin, B. F.; and Mikhaleva, N. P. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 13, 1969, pp 99-107.

44. Barbashova, Z. I.; Zhukov, Ye. K.; Baklanova, S. M.; et al. in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii," Novosibirsk, 1970, pp 26-35.

45. Ryl'nikov, Yu. P., and Fedorov, I. V. in "Povolzhskaya konf. fiziologov s uchastiyem biokhimikov, farmakologov i morfologov. 6-ya. Materialy" [Proceedings of 6th Povolzh'ye Conference of Physiologists, With the Participation of Biochemists, Pharmacologists and Morphologists], Cheboksary, Vol 2, 1973, p 126.

46. Starostin, V. I.; Portugalov, V. V.; and Il'ina-Kakuyeva, Ye. I. DOKL. AN SSSR, Vol 190, No 5, 1970, pp 1215-1217.

47. Lobova, T. M. KOSMICHESKAYA BIOL., No 5, 1973, pp 32-35.

48. Fedorov, I. V.; Ryl'nikov, Yu. P.; and Lobova, T. M. KARDIOLOGIYA [Cardiology], No7, 1973, pp 50-54.

49. Ryl'nikov, Yu. P. KOSMICHESKAYA BIOL., No 2, 1974, pp 8-13.

50. Sidorenkov, I. V., and Gil'miyarova, F. N. VOPR. MED. KHIMII, No 3, 1969, pp 250-253.

EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

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RESULTS OF STUDIES OF PULSED BLOOD FLOW AND REGIONAL VASCULAR TONUS DURING FLIGHTS IN THE FIRST AND SECOND EXPEDITIONS ABOARD THE SALYUT-6--SOYUZ ORBITAL COMPLEX

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[Article by V. F. Turchaninova and M. V. Domracheva, submitted 10 May 79]

[English abstract from source]

The dynamics of pulse blood filling and regional vascular tone was studied in the crewmembers of 96- and 140-day flights aboard the station Salyut-6 — Soyuz. Measurements were taken before, during and after flights, using a specially designed tetrapolar rheograph. Rheograms of the torso, forearms, legs, and rheoencephalograms of the right and left hemispheres in the frontal-mastoidal lead were recorded. The results showed that in zero-g the cosmonauts developed typical hemodynamic changes indicative of cephalad blood shifts. Thus, the hypothesis advanced and theoretically substantiated previously has found further support.

[Text] The conception has been formed at the present time that there is redistribution of fluids, particularly blood, in a cranial direction in the human body in weightlessness. This hypothesis was based primarily on the sensations of a rush of blood to the head, which cosmonauts experience, as well as theoretical analysis of the influence of weightlessness on human functional systems. In addition, some objective data were obtained during flights: shifting of the center of mass toward the head, demonstrated by photography of facial puffiness in infrared light, dilatation of veins in the upper part of the body, reduction in diameter of the lower limbs and in size of the legs and thighs on the 3d flight day [1]. Arteriovenous pulsography demonstrated increased filling and pressure of jugular veins [2, 3].

Our objective here was to study the dynamics of pulsed blood flow [filling] and regional tonus of different parts of the body in the course of 96- and 140-day flights.

Methods

Rheograms of the trunk, arm and leg, at rest, were taken with a specially developed tetrapolar rheograph before, during and after space flights, as well as rheoencephalograms. The onboard rheograph records not only the rheographic curve, but a calibration signal that is proportionate to the value of the constant component of impedance. In accordance with this arrangement of the instrument, determination of the index of pulsed filling ($PF = \Delta R/R$) is made by finding the ratio of rheogram amplitude to the calibration signal ($\Delta R/R = A/K \cdot const$); the value of the constant depends on the region examined, and it is given in the technical specifications of the instrument. Another distinction of this instrument is that the required amplification and range of measurement of R/R is made by altering the position of the switch for modes of instrument operation.

Background studies were made at different stages of the preflight period. During the flights, the rheogram of the trunk and rheoencephalogram were recorded at approximately the same intervals throughout the period of weightlessness. Rheograms of the extremities were recorded on the 14th and 24th days for the crew of the first expedition; on the 21st, 68th, and 110th days for the commander in the second expedition, 4th, 63d and 119th days for the flight engineer in the second expedition.

When interpreting the rheograms, in addition to the pulsed and minute flow indices, we calculated the conventional indices of tonus of vessels of different caliber. In addition, we determined cardiac stroke volume (SV) and minute volume of circulation (MV) using the formula of A. A. Kedrov [4, 5].

Results and Discussion

SV increased in 3 out of 4 comsonauts on the 4th-7th flight days. Thereafter, there were usually insignificant fluctuations, and more significant deviations were only observed in a few cases: SV increased by 25% on the 82d day in the commander of the first expedition; it decreased by 25% on the 63d day in the commander and on by 28% on the 119th day in the flight engineer of the second expedition. At the same time, SV was essentially somewhat low throughout the flight of the flight engineer of the first expedition (by 2-15%). In virtually all of the cosmonauts, MV exceeded the mean preflight level or did not differ from it. After the flights, there was prevalence of low SV and MV in the crew of the first expedition as well: the levels were not restored for 11 days.

Figures 1 and 2 illustrate the dynamics of filling of vessels of the head, showing that pulsed and minute filling of cerebral vessels as increased in both cosmonauts (more so in the flight engineer) during the 96-day mission, and did not diminish by the end of the flight. During the 140-day mission, we also observed an appreciable increase in filling of cerebral vessels which, however, did not differ from the preflight level or even diminished during the second half of the mission. The interhemispheric asymmetry of filling observed about half way through the flight decreased or disappeared entirely by the end of the mission. Filling remained increased in the crew of the first expedition on the 3d postflight day, and it did not present positive dynamics in the flight engineer. Filling with blood increased by 55-65% in the commander and decreased by 55-67% in the flight engineer on the 9th day after the 140-day mission.

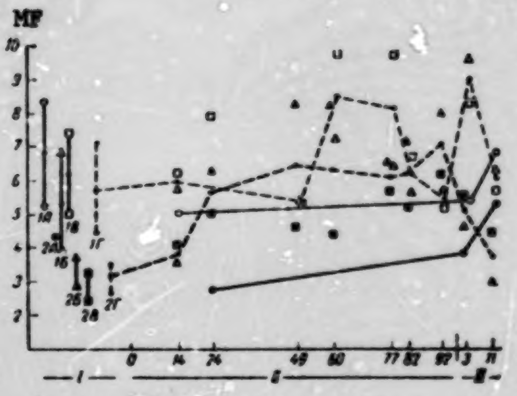

Figure 1.
Dynamics of filling of vessels of the brain and leg in the commander (1) and flight engineer (2) of the first main expedition
Here and in Figure 2:
A) index of filling of leg vessels
Б) index of filling of right hemisphere vessels
B) index of filling of left hemisphere vessles
Г) mean filling index for vessels of right and left hemispheres
I) before flight
II) during flight
III) after flight
MF) index of minute filling with blood

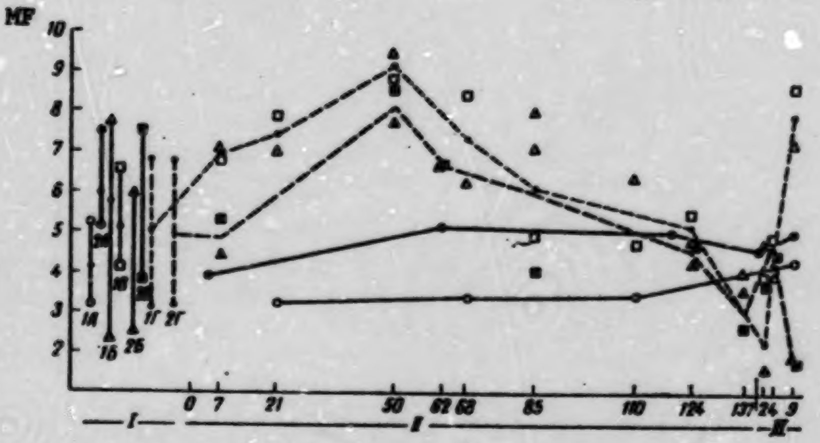

Figure 2. Dynamics of indices of vascular filling in the brain and leg of commander (1) and flight engineer (2) in second main expedition

There was less filling with blood of leg vessels during the flight and on the 2d-3d postflight day than before it. There was a mild tendency toward normalization thereof in the second half of the flight of cosmonauts participating in the second expedition (see Figures 1 and 2). At the same time, flow to the forearm exceeded the preflight level or did not differ from it, whereas on the 2d-3d postflight day it usually diminished somewhat.

In three out of four cosmonauts, arteriolar and venous tonus of cerebral vessels essentially diminished during the flights, and in some cases quite significantly, which was manifested by a change in form of the rheoencephalograms (the notch shifted below the isoelectric line). At the same time, there was no consistent pattern to changes in tonus of small vessels in the flight engineer of the second expedition, and its indices were within the range of preflight levels. After the mission, arteriolar tonus usually remained diminished, and it increased in only one cosmonaut. In addition, venous tonus decreased only in the crew of the first expedition, and it did not recover on the 11th day. The changes in arteriolar and venous tonus of the forearm and leg of different cosmonauts were individual in nature; however, in most cases there was a pattern, as manifested by opposite dynamics of tonus of small vessels of the forearm and leg. After the flight, tonus of arterioles and veins of the forearm diminished in three cosmonauts, whereas in the flight engineer of the second expedition it increased, with concurrent increase of tonus in the legs of all crew members.

Thus, according to the rheographic findings, there was expression of the following changes in central and regional hemodynamics: initial (4th-7th days) increase in SV in 3 out of 4 cosmonauts; a tendency for MV to exceed preflight levels throughout the flight and decrease in volume of circulation after the flight; increased pulsed and minute filling of cerebral vessels, which reverted to preflight levels after 85-110 days of the 14-day mission; both parameters remained high after the 96-day flight and diminished after the 140-day flight; appearance of marked asymmetry of filling of cerebral vessels on the 49th-77th day in the first crew and on the 85th flight day in the second crew, with equalization by the end of the flight; decreased filling of leg vessels during and after flight, with concurrent increase or absence of change in filling of forearm vessels (only during flight); diminished arteriolar and venous tonus of cerebral vessels of three cosmonauts during and after flight; changes in different directions in arteriolar and venous tonus in the forearm and leg, the deviations being individual in nature in different crew members.

The changes in central and regional hemodynamics during the space flights may be attributable to several factors, the chief ones being redistribution of blood and functional loads on vessels of different parts of the body, development of deconditioning of muscles and decreased role thereof as a venous pump. According to current conceptions [6, 7], in weightlessness blood and tissular fluid shift in a cranial direction, and this probably leads to the initial increase in SV and MV demonstrated in our studies. Perhaps, this is also related to the increase in pulsed flow to cerebral vessels with concurrent decrease in pulsed flow to the leg. In view of the fact that the rheographic studies were made starting only on the 4th-7th days, the decrease in arteriolar and venous tonus of cerebral vessels may be interpreted as the result of an adaptive reaction helping to imporve efflux of blood and preventing development of venous stasis. Dilatation of the atria and central veins due to the hemodynamic changes at the early stage of weightlessness apparently leads to subsequent decrease in circulating blood volume, which has been found in a number of postflight studies [8]. We cannot rule out the possibility that this is the cause of normalization of SV, which developed by the end of the 2d-3d weeks of the flights.

A comparison of our results to those of model studies (antiorthostatic [head down] hypokinesia for 49 days) revealed that the reaction referable to SV during the flights and with exposure to factors simulating weightlessness was in approximately the same direction and of the same duration. As for increased filling of cerebral vessels, the increment was more marked during the flight and normalization occurred only on the 85th-110th days. All this warrants the conclusion that the redistribution of blood in a cranial direction in weightlessness is more persistent and associated with greater increase in pulsed filling of cerebral vessels, against the background of significant decline of indices of arteriolar and venous tonus, than observed under antiorthostatic hypokinetic conditions with a -4° tilt.

The causes of the observed asymmetry in filling of vessels of the right and left hemispheres in some of the in-flight studies are not quite clear. We can only assume that the observed asymmetry reflects individual distinctions of anatomical structure, vascular tonus and reactivity, which become more marked or are manifested only when there is considerable increase in filling. Moreover, the opinion is held that asymmetry of filling of cerebral vessels may be indicative of development of vegetovascular dysfunction, i.e., more or less marked changes in function of vasomotor centers [9]. However, this hypothesis requires verification.

Thus, the existing hypothesis of redistribution of blood in the human body under the influence of weightlessness has obtained additional confirmation.

BIBLIOGRAPHY

1. Thornton, W. E.; Hoffler, G. W.; and Rummel, J. A. in "Skylab Life Sciences Symposium Proceedings," Houston, Vol 11, 1974, pp 211-232.

2. Yuganov, Ye. M.; Degtyarev, V. A.; Nekhayev, A. S.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1977, pp 31-37.

3. Degtyarev, V. A.; Nekhayev, A. S.; Bednenko, V. S.; et al. Ibid, No 4, 1979, pp 8-12.

4. Kedrov, A. A. KLIN. MED. [Clinical Medicine], No 1, 1941, pp 71-76.

5. Idem, Ibid, No 5, 1948, pp 266-271.

6. Gazenko, O. G.; Gurovskiy, N. N.; Bryanov, I. I.; et al. in "Simpozium po kosmicheskoy biologii i meditsine. 10-y. Tezisy" [Summaries of Papers Delivered at 10th Symposium on Space Biology and Medicine], Moscow, 1977, pp 13-14.

7. Kovalenko, Ye. A. in "Nevesomost'" [Weightlessness], Moscow, 1974, p 243.

8. Johnson, R. L. in "Man in Space," Moscow, 1974, pp 142-159.

9. Yarullin, Kh. Kh., and Vasil'yeva, T. D. KOSMICHESKAYA BIOL., No 3, 1977, pp 20-26.

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CIRCULATION IN EXERCISING CREW MEMBERS OF THE FIRST MAIN EXPEDITION ABOARD SALYUT-6

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[Article by V. S. Georgiyevskiy, N. A. Lapshina, L. Ya. Andriyako, L. V. Umnova, V. G. Doroshev, I. V. Alferova, V. N. Ragozin and Ye. A. Kobzev, submitted 26 Dec 78]

[English abstract from source]

During the 96-day flight aboard the Salyut-6 station the crewmembers showed a satisfactory response to bicycle ergometry of moderate load. However, cardiovascular regulation during exercise declined, particularly by the end of the first and the beginning of the second month. This was mainly associated with deconditioning due to an inadequate work load. Its increase helped to restore an initial level of circulation during exercise by the end of the mission.

[Text] Since the first missions, exercise was used extensively in clinical and physiological studies of cosmonauts, and later aboard the Salyut and Skylab orbital stations [1-5]. This article deals with a study of the changes in the cardiovascular system during exercise in the course of a 96-day orbital flight.

Methods

An onboard bicycle ergometer was used for the physical load test. The subjects had to perform exercise constituting 3750 kg-m within 5 min of pedaling at a mean rate of 750 kgm/min and speed of 60 r/min. It actually fluctuated on different test days from 3010 to 4050 kg-m in the commander and flight engineer, i.e., it was on the level of average load.

Polynome-2M equipment was used to record the tachooscillogram, kinetocardiogram from the region of the apex beat and sphygmogram of the femoral artery [6]. Mean dynamic, lateral systolic, end systolic and pulse arterial pressure (AP) were determined from the tachooscillogram. The kinetocardiogram served to find isovolumetric contraction (IC) and period of ejection (PE) for the left ventricle. We measured the pulse wave velocity (PWV) over the descending aorta. We calculated stroke (SV) and minute (MV) volumes of circuation, specific real resistance (SAR), ejection of minute blood volume (EMBV), interphase (IF) and intrasystolic (IS) indices. The parameters were recorded before and within 2-3 min after pedaling. In addition, there was continuous monitoring of heart rate (HR) and recording of the EKG in the DS lead.

Results and Discussion

Both cosmonauts tolerated the exercise tests satisfactorily throughout the flight aboard the orbital station: they felt well; they did not experience pain or other unpleasant sensations. However, immediately after they stopped pedaling, the cosmonauts had the feeling of blood rushing to the head, and there were signs of intensive regulation of circulation.

The most marked cardiovascular reactions were demonstrated in both cosmonauts on the 24th flight day. In spite of the fact that pedaling time was reduced to 3 min 18 s for the commander and to 4 min 30 s for the flight engineer, maximum HR increased to 144 and 145/min, respectively (before the flight, this parameter constituted 138 and 114/min). A "stable state" was not reached with respect to pulse rate. In the flight engineer, lateral systolic and particularly end systolic AP were above preflight levels. There was also relative increase in IC, decrease in PE, increase in IF and decrease in IS (see Table).

It should be noted that the first signs of change in regulation of circulation were demonstrable already on the 7th flight day, although the test was well-tolerated at that time. As a result of the physical load, there was an increase by more than 4 m/s in PWV, although it had also been somewhat higher than the preflight level before the test. AP dropped as a result of exercise in the commander. In addition, we observed stepped change in end systolic AP (in the 2d min after the load it was lower than in the 3d), which is usually related to overfatigue or stress [7]. The nature of the AP reaction did not change in the flight engineer.

Of special interest are the dynamics of duration of the PE period. As a result of the exercise, it became shorter in the commander, both as compared to the level on the ground and appropriate level. We had observed significant shorting of the PE and relative extension of IC after exercise in our previous studies [2, 3], and we interpreted this as a signed of decreased venous return. The decrease in IS and EMBV was indicative of the same thing.

According to the general hemodynamic indices, we could assume that endurance of the test by the commander improved on the 42d day. In spite of the increase in amount of exercise to 4050 kg-m, maximum HR during exercise. AP and PWV after it corresponded to preflight levels. However, there were changes in intracardiac hemodynamics indicative of decreased venous return.

Circulatory parameters during test on bicycle ergometer

Period	Time after pedaling, min	HR/min	AP, mm Hg				IC, s	PE, s	PWV, m/min	SV, mℓ	MV, ℓ/min
			minimum	mean dynamic	lateral systolic	end systolic					
					Commander						
Before flight	BG	64	71	98	121	150	0,050	0,284	6,0	123	7,5
	1	75	79	104	135	166	0,035	0,230	8,0	80	6,0
	2	70	80	96	122	154	0,030	0,250	9,1	57	4,0
Weightlessness, days: 7th	BG	68	78	113	132	153	0,060	0,262	10,0	69	4,4
	1	96	—	—	—	—	0,030	0,185	—	—	—
	2	67	74	103	124	144	0,030	0,235	14,6	36	2,4
24th	BG	58	68	100	115	153	0,060	0,300	4,9	145	8,5
	1	90	70	109	140	172	0,035	0,185	7,7	83	7,5
	2	74	68	98	128	155	—	0,250	6,1	126	9,3
42d	BG	68	63	89	108	140	0,054	0,287	6,1	111	7,6
	1	111	81	107	125	175	0,042	0,225	8,9	68	7,6
	2	78	74	98	125	158	0,040	0,255	8,1	85	6,6
70th	BG	72	69	96	115	150	0,055	0,245	7,0	81	5,8
	1	114	78	109	125	180	0,038	0,224	—	—	—
82d	BG	64	66	102	112	150	0,040	0,280	5,8	113	7,3
	1	86	65	111	127	175	0,037	0,220	9,1	78	6,7
	2	77	80	115	130	160	—	—	—	—	—
					Flight engineer						
Before flight	BG	51	63	90	116	143	0,055	0,316	7,4	118	6,0
	1	70	74	93	136	167	—	—	—	—	—
	2	67	70	94	130	176	0,030	0,270	8,4	102	6,8
Weightlessness, days: 7th	BG	60	66	84	108	139	0,057	0,280	8,15	75	4,5
	1	90	60	89	114	162	0,030	0,170	11,7	64	5,8
	2	74	58	87	112	147	—	0,240	12,5	54	4,0
24th	BG	56	58	78	98	128	0,051	0,300	5,8	119	6,6
	1	120	68	100	135	180	0,037	0,180	11,6	60	7,2
	2	97	70	97	122	180	—	0,194	11,9	46	4,4
42d	BG	64	62	83	99	138	0,053	0,300	6,8	91	5,8
	1	86	65	87	111	168	0,030	0,230	9,4	63	5,5
	2	78	63	84	105	152	—	0,254	10,0	60	4,7
70th	BG	67	66	88	104	142	0,056	0,284	5,8	110	7,3
	1	105	68	100	122	180	0,045	0,180	10,0	53	5,5
	2	98	66	90	112	178	0,047	0,225	8,5	71	7,0
82d	BG	64	60	82	97	130	0,049	0,289	5,9	95	6,0
	1	114	70	95	124	174	0,035	0,228	9,7	84	9,6
	2	96	72	95	122	175	0,035	0,237	8,8	80	7,6

Key: BG) background

On the 42d flight day, the flight engineer performed less exercise (2495 kg-m). His circulatory reaction was poorer than before the flight; as a result of exercise HR increased, while PE decreased.

There was substantial improvement of the commander's endurance of the test on the 70th and 82d flight days, as compared to the preceding tests. The main circulatory parameters were close to preflight levels. However, there were some elements inherent in unstable reactions. With lower values for lateral systolic, dynamic mean and minimum AP, there was a high end systolic level and relatively higher PWV.

On the 70th day, the flight engineer increased the pedaling rate to the specified level and maintained it rather well for the entire 5 min; however, his circulatory reaction was somewhat poorer than before the flight. By the 82d day, he presented significant improvement of circulatory regulation during exercise. Circulatory parameters came close to preflight levels, although we did observe a somewhat higher HR, end systolic AP, PWV and somewhat lower SV, IC and PE.

Special mention should be made of the fact that, at this time, there was restoration in both cosmonauts of the preflight correlation between duration of IC and PE, i.e., the syndrome of myocardial hypodynamia disappeared.

It may be assumed that deconditioning was the chief cause of poorer endurance of the exercise test. As we have already noted, the first signs thereof were noted in the commander on the 7th flight day. Distinct signs of deconditioning developed on the 24th and 42d days. On these days, in spite of the decrease in amount of exercise, there was a substantial increase in HR, slower build-up of pedaling rate, elevation of AP and decrease in SV, as well as appearance of signs of diminished venous return. This stage of the flight was characterized by an increase in volume of work related to operation of the station, as a result of which there was a certain disruption of the work and rest schedule and, in particular, a decrease in physical exercise, as compared to the planned amount. Subsequent improvement of regulation of the cardiovascular system with the load on the 70th and 82d days was obtained by increasing the intensity of exercise with optimization of the work and rest schedule. Analogous findings were also made previously [1, 3].

Thus, the test on a bicycle ergometer enabled us to demonstrate deterioration of the reaction of the cardiovascular system to a physical load. Maximum changes were observed by the end of the 1st and start of the 2d month, whereas at the end of the flight the reaction was close to the preflight level. The poorer regulation of circulation was related primarily to deconditioning, due to an inadequate amount of physical exercise. It is imperative to implement the entire complex of preventive measures to maintain a high level of fitness.

BIBLIOGRAPHY

1. Rudnyy, N. M.; Gazenko, O. G.; Gozulov, S. A.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1977, pp 33-41.

2. Doroshev, V. G.; Batenchuk-Tusko, T. V.; Lapshina, N. A.; et al. Ibid, No 2, pp 26-31.

3. Degtyarev, V. A.; Doroshev, V. G.; Kalmykova, N. D.; et al. Ibid, No 3, 1978, pp 15-20.

4. Bergman, S. A.; Hoffler, G. W.; and Johnson, R. L. in "Skylab Life Symposium. Proceedings," Houston, Vol 11, 1974, pp 255-283.

5. Michel, E. L.; Rummel, J. A.; Savin, Ch. F.; et al. Ibid, pp 297-336.

6. Degtyarev, V. A.; Doroshev, V. G.; Kalmykova, N. D.; et al. KOSMICHESKAYA BIOL., No 2, 1974, pp 34-42.

7. Kukolevskiy, G. M. in "Serdtse i sport" [The Heart and Sports], Moscow, 1968, pp 303-331.

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HEMODYNAMICS AND PHASE STRUCTURE OF THE CARDIAC CYCLE IN MEMBERS OF THE FIRST CREW OF SALYUT-5 AT REST

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[English abstract from source]

In the Salyut-5 flight studies of circulatory functions were continued. Heart rate, arterial pressure, time intervals of the left and right ventricles were measured at rest. Peripheral resistance and cardiac output were calculated. At early flight stages cardiovascular changes occurred due to an increased blood inflow to the heart. During the second half of the mission cardiac output and arterial pressure remained elevated, as fatigue of the cosmonauts increased.

[Text] The study of circulation at rest in the first crew of the Salyut-5 orbital station is a continuation of the programs dealing with the study of the effects of space flight factors on the human body [1, 2]. In spite of the fact that a certain amount of data has been accumulated [3-6], the distinctions of hemodynamic changes in weightlessness require further investigation. This is attributable to the fact that each successive flight is experimental and contains new elements. There are changes in the cyclogram of crew work, work and rest schedule, conditions under which experiments are conducted, scope thereof, etc. As in all experimental work, elements of risk are retained. All this makes it difficult to interpret data and single out the specific changes that are related to the direct effect of weightlessness. Adherence to standard examination conditions, which could provide for good comparability of findings from studies conducted at different stages of a flight, constitutes an extremely difficult task.

Methods

Polynome-2M equipment was used for morning, daytime and evening studies before conducting functional tests involving lower body negative pressure (LBNP) and a physical load. Data were obtained for the flight engineer under basal metabolic conditions on the 40th day of the flight. The second crew member placed the sensors and adjusted equipment 20-30 min before the start of a telemetric communication session. A record was taken of the tachooscillogram of the brachial artery, kinetocardiogram (KKG) from the region of the apex beat and 4th intercostal space on the right, near the sternum, and sphygmogram of the femoral artery. We determined the heart rate (HR), minimum (AP_m), mean (AP_a), lateral (AP_1) and end (AP_e) systolic arterial pressure, pulse wave velocity (PWV) in the aorta, duration of isometric contraction (IC) and period of ejection (E) of blood by the ventricles, as well as interphase coefficient K [3]. We used the Bremse-Ranke formula to calculate stroke and minute volumes (SV, MV), and the method of N. N. Savitskiy [7] for determination of actual and working (proper) peripheral resistance (APR, WPR).

Results and Discussion

The distinctive feature of the cosmonauts' mission was that they performed very intensive work. The cosmonauts worked more on their own initiative than provided in the program. This resulted in reduction of time reserved for rest, meals and physical exercise. As a result, the crew members developed considerable fatigue, which was associated with substantial sleep disorders. Overall shortage of sleep constituted more than 100 h for both cosmonauts during the 49-day mission.

HR did not exceed preflight levels in the commander after the 4th day of the flight, whereas in the flight engineer it was lower by a mean of 8% than the initial level for the first 2 weeks of the mission and later exceeded the initial level by a mean of 29% (Table). We know from the prior flights that AP levels, particularly AP_1 and AP_e, usually were 10-15 mm Hg higher for the first 2 weeks. Thereafter, as the cosmonauts adjusted to weightlessness, AP had a tendency toward normalization [1-3, 5, 6]. The commander's AP did not drop during the flight. The increment of AP_a and AP_e constituted a mean of 11% during the flight and AP_1 23%. In most cases, AP_m corresponded to the preflight level. The greatest elevation of all AP levels of the commander was observed on the 14th flight day, when he performed the work program of both crew members by himself. In the flight engineer, AP_m and AP_a remained at the prefight level, while AP_1 and AP_e rose by a mean of 15%. Pulse pressure rose by a mean of 35% in both cosmonauts. The circulatory changes we observed resembled, to some extent, the dynamics of HR and AP of the commander of the Salyut-1 spacecraft and several American astronauts [1, 3, 6]. Berry [9] attributed this to the so-called "commander effect." He believed that the more frequent elevation of AP in spacecraft commanders was related to their special responsibility for performance of the program of the mission. Unfortunately, American researchers do not measure SV and MV in weightlessness.

Hemodynamic parameters of resting Salyut-5 crew members

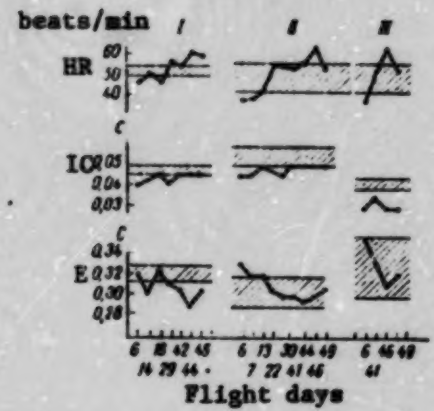
Time of study	HR	AP_m	AP_a	AP_1	AP_e	PWV, m/s	SV, mℓ	MV, ℓ	APR, arbitr. units
Commander									
Before flight	50	59	85	105	128	6,4	105	5,2	31
Flight days:									
6th	47	54	96	119	146	6,3	157	7,6	25
14th	50	70	96	132	153	6,9	135	6,7	27
16th	48	63	94	125	140	6,1	160	7,7	25
28th	56	65	96	126	148	6,5	145	8,1	23
46th	53	67	92	121	147	7,0	118	6,3	27
After flight (4th day)	59	63	90	113	132	5,9	130	7,6	22
Flight engineer									
Before flight	44	50	73	90	116	5,3	102	4,5	102
Flight days:									
6th	40	48	75	109	131	6,5	138	5,5	26
7th	41	48	72	100	132	6,6	121	5,0	27
13th	41	51	87	110	137	6,3	134	5,5	30
21st	55	48	—	98	130	6,0	128	7,0	—
28th	51	50	80	105	140	5,8	137	7,0	22
40th*	53	42	75	100	122	5,2	166	8,8	18
43d	58	57	79	106	132	6,1	121	7,0	26
After flight (4th day)	52	62	112	138	4,7	162	8,4	20	

Note: The asterisk refers to data obtained under basal metabolic conditions.

In the first month of the flight, the commander's SV was a mean of 46% greater than the preflight value and MV was 30% greater. It is only by the 46th day that circulation volumes decreased significantly, although they did not reach preflight levels. In the flight engineer, SV was 20% or more above the preflight level. For the first 2 weeks, MV was 10-20% above the preflight level. Thereafter, the differences constituted up to 50%.

In the commander, PWV remained in the range of preflight levels. In the flight engineer, the highest PWV was found at the first stage of the flight. From the 13th flight day on, PWV gradually decreased, remaining higher, on the average, than the preflight level.

APR of the commander decreased by 15% during the flight; however, the difference between APR and WPR exceeded +15% up to the 27th flight day, which was an indirect indication of some increase in arteriolar tonus. On the 44th day, APR conformed with the proper level. In the flight engineer, it was the same as before the flight for the first 2 weeks of flight, then decreased by 30%. On the 7th and 40th flight days, the difference between APR and WPR constituted 17%, i.e., vascular tonus was decreased on these days.



Dynamics of phases of the left ventricle for commander (I) and flight engineer (II), and right ventricle for flight engineer (III) during flight. The striped area indicates the range of preflight figures

The shape of the KKG of the apex of the heart and from the 4th intercostal space to the right of the sternum corresponded to the findings on the ground. There were two stages of changes in phase structure of the cardiac cycle. The first stage (6th-16th days for the commander and 6th-13th days for the flight engineer) was characterized by some slowing of the pulse, longer period of ejection and mechanical systole of the left ventricle in relation to proper values. Coefficient K changed particularly distinctly in the flight engineer due to some extension of the ejection period and shortening of the period of isovolumetric contraction (see Figure). Examination of phases of the right ventricle of the flight engineer, made on the 6th flight day, yielded analogous findings.

At the second stage, starting on the 22d flight day, the flight engineer presented reduction of ejection period and mechanical systole to the bottom preflight range against the background of higher HR. In the commander, the ejection period and mechanical systole decreased even more starting on the 29th day; however, the duration of these phases in both cosmonauts virtually corresponded to the proper values. The duration of isometric contraction and coefficient K increased, as compared to the first stage of the flight. Examination of duration of right ventricular phases in the flight engineer at the end of the flight (41st, 46th and 49th days) also revealed shortening of the ejection period and mechanical systole, as compared to the values obtained at the start of the flight.

Evidently the differences in dynamics of circulatory parameters of the crew members were attributable to their individual adaptability to the drastically changing working conditions on the station. During the period between the 21st and 30th days, when the "sleep-waking" cycle was shifted by almost 6 h in both directions, the commander developed a vegetovascular crisis [8]. Thereafter, additional rest time was granted to the crew, and the commander was able to sleep for 30-40 min in the daytime. As a result, the cosmonaut felt better. By the end of the mission, his circulation volume decreased substantially. There was no normalization of impaired sleep for the flight engineer. Signs of fatigue progressed, and headache was added to them. Perhaps, deterioration of general condition and diminished fitness for work in the flight engineer were due to the disturbances in regulation of vascular tonus. Examination of the cosmonaut at this time revealed great lability of AP and a substantial increase in MV, that were inconsistent with his state of rest. Even under close to basal metabolic conditions (40th day), SV and MV were significantly higher than preflight levels. PWV decreased, while the difference between APR and WPR exceeded 15%, which was indicative of relative decrease in vascular tonus. A comparison of rheographic data on the 26th and 46th flight days revealed an increase in venous components and signs of decreased arterial tonus in the fronto-occipital lead in the light engineer. During this period, he had less endurance for the functional tests with exercise and LBNP.

Thus, the first crew of Salyut-5, unlike all crews that had previously flown aboard orbital stations, presented relatively greater elevation of circulatory indices in weightlessness, without overt regression with increase in duration of the flight. With constant exposure to space flight factors, the marked circulatory reaction, inconsistent with rest, probably reflected the cosmonauts' increasing fatigue and development of close to pathological states. The obtained data expand existing conceptions of the distinctions and criteria for evaluating adjustment of cosmonauts at different stages of flight.

BIBLIOGRAPHY

1. Degtyarev, V. A.; Doroshev, V. G.; Kalmykova, N. D.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1974, pp 34-42.

2. Doroshev, V. G.; Batenchuk-Tusko, T. V.; Lapshina, N. A.; et al. Ibid, No 2, 1977, pp 26-31.

3. Degtyarev, V. A.; Popov, I. I.; Batenchuk-Tusko, T. V.; et al. in "Nevesomost'" [Weightlessness], Moscow, 1974, pp 132-157.

4. Degtyarev, V. A.; Doroshev, V. G.; Batenchuk-Tusko, T. V.; et al. KOSMICHESKAYA BIOL., No 3, 1977, pp 26-31.

5. Itsekhovskiy, O. T.; Polyakova, A. P.; and Lyamin, V. R. Ibid, No 2, pp 37-42.

6. Vorob'yev, Ye. I.; Gazenko, O. G.; Gurovskiy, N. N.; et al. Ibid, No 5, 1976, pp 3-18.

7. Savitskiy, N. N. "Biophysical Bases of Circulation, and Clinical Methods of Studying Hemodynamics," Leningrad, 2d edition, 1963.

8. Rudnyy, N. M.; Gazenko, O. G.; Gozulov, S. A.; et al. KOSMICHESKAYA BIOL., No 5, 1977, pp 33-41.

9. Berry, Ch. A. in "Man in Space," Moscow, 1974, pp 51-70.

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EFFECT OF WEIGHTLESSNESS AND ARTIFICIAL GRAVITY ON ION-REGULATING FUNCTION OF RAT KIDNEYS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 21-25

[Article by Ye. A. Il'in, Yu. V. Natochin, N. A. Ilyushko, Yu. I. Kondrat'yev, V. T. Bakhteyeva, Ye. M. Gazhala, O. A. Goncharevskaya, Ye. A. Lavrova and Ye. I. Shakhmatova, submitted 13 Feb 79]

[English abstract from source]

Weightless rats showed greater changes in the fluidelectrolyte metabolism and ion regulatory function of the kidneys than centrifuged rats. During water loads they exhibited an increased sodium excretion. During potassium loads they displayed a higher potassium excretion. The study of electrolyte composition of different kidney segments demonstrated a reduced potassium content in the wet cortical and medullary matter due to elevated tissue hydration. Kidney microdissection did not reveal any structural differences in nephrons of the weightless and centrifuged rats.

[Text] Man's exposure to space flight conditions is associated with significant changes in fluid-electrolyte metabolism and renal function [1-3]. Studies involving the use of functional load tests revealed substantial changes in systems of regulation of fluid-electrolyte metabolism in man under weightless conditions [7].

In this article, we studied the reaction of kidneys and systems of their regulation to a water and potassium load, we measured the electrolyte composition of different parts of the kidney and performed microdissection of the kidney in experiments on rats aboard Cosmos-936 biosatellite, for the purpose of analyzing the physiological mechanisms of the effect of weightlessness on ion-regulating renal function.

Methods

We used in the experiment 15 Wistar SPF rats (5 rats were submitted to weightlessness, 5 to artificial gravity, and a synchronous control experiment was conducted with the other 5). The flight and synchronous experiments lasted 18.5 days. All three groups of animals were fed the same diet of feed in paste form at the rate of 40 g/day.

Tests with a water load (5 mℓ/100 g weight) were conducted on the 1st and 4th days after the flight and synchronous experiments, and tests with a load of 1.25% KCl solution (5 mℓ/100 g weight) on the 2d and 5th days. After the water and salt loads, urine was collected every 30 min for 4 h. We assayed in all urine samples the concentration of sodium and potassium using a flame photometer, calcium and magnesium concentration using an atom-absorption spectrophotometer. Studies of electrolyte composition of different parts of the kidney (cortex, external medullary layer, renal papilla) were made after ashing the samples with concentrated HNO_3. For microdissection of the kidney, it was macerated in HCl, then whole superficial, intracortical and juxtamedullary nephrons were isolated.

Results and Discussion

Elimination of water load: The test with a water load was conducted to evaluate the osmoregulatory system and possible fluid deficiency in the organism. Elimination of the water load was at a maximum in rats submitted to weightlessness, on the first day after the experiments (Figure 1). On the 4th day of the recovery period, fluid elimination after the water load was reliably lower in flight animals than those of the synchronous experiment. A comparison of the dynamics of development of the diuretic reaction and level of maximum diuresis in the three groups of animals failed to demonstrate reliable differences.

Analysis of ionograms of urine after the water load is of substantial significance to evaluation of the condition of the kidneys and osmoregulatory system. In rats that had been submitted to weightlessness, we demonstrated maximum elimination of sodium (see Figure 1) on the 1st day of the readaptation period. We failed to demonstrate differences in elimination of potassium, calcium and magnesium in the three groups. On the 4th day of the readaptation period, elimination of sodium and potassium after the water load was reliably lower in flight rats than in animals used in the synchronous experiment.

Elimination of potassium load: The studies of excretion of potassium loads after a space flight, which were conducted on animals for the first time, were of great interest to characterization of potassium metabolism. Intake of potassium led to virtually the same increase in elimination of fluid in animals involved in the flight and synchronous experiment (Figure 2). On the 5th day of readaptation, excretion of fluid after the potassium load was reliably lower in flight animals than those in the synchronous experiment. On the 2d day of readaptation, excretion of potassium was highest in flight animals exposed to weightlessness. On the 5th day after landing there were no differences between all three groups with regard to excretion of potassium after a potassium load (see Figure 2).

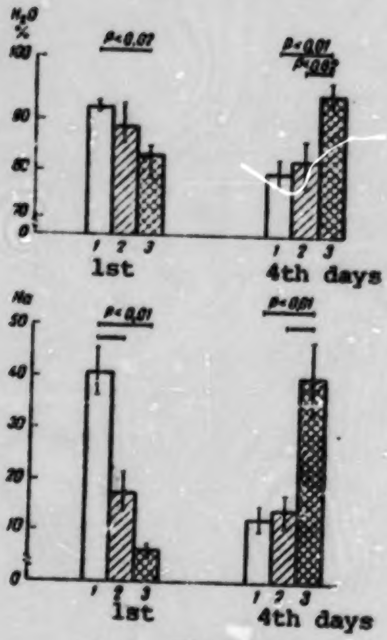

Figure 1.
Excretion of fluid (% of given volume) and sodium (in μeq/100 g weight in 4 h) after water load

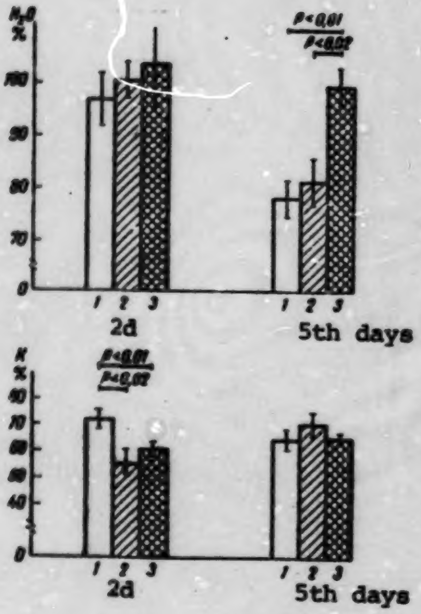

Figure 2.
Excretion of fluid (% of given volume) and potassium (% of given quantity) after potassium load

Key to both figures:
1) flight, weightlessness 2) flight, centrifuge 3) synchronous experiment

Excretion of sodium, potassium and magnesium after a potassium load was virtually the same in all three groups of animals on the 2d day of the readaptation period. On the 5th readaptation day, excretion of sodium was reliably lower in flight animals than those of the synchronous experiment.

Microdissection of the kidney: It can be assumed that the above-mentioned changes in renal reactions to the tests are related either to structural and biochemical changes in renal tissue, or change in regulatory mechanisms. Hypotheses have been expounded previously that space flights can lead to stasis in urinary tubules and deformation thereof. For this reason, we performed microdissection of the kidneys and isolated nephrons. The obtained results failed to demonstrate any differences whatsoever in structure of different parts of neprhons of all populations after the flight.

Electrolyte composition of different parts of the kidney: Assay of sodium and potassium in the cortex and medullary substance of the kidney enabled us to determine the gradient created by the function of the reflux system and to tentatively evaluate the changes in cellular concentration of potassium, since tissular potassium is determined primarily by the level of cellular potassium. The most substantial differences were found in potassium content of different parts of the kidney (see Table). After exposure to weightlessness, it was reliably lower (as compared to indices for the synchronous experiment) in wet cortical substance ($P<0.001$), external and internal (papilla) medullary substance ($P<0.01$). The changes were less marked in rats kept in a centrifuge during the flight than in control animals. They were not demonstrable in the renal cortex, but only found in the medullary layer ($P<0.05$).

Electrolyte composition of different parts of the kidney (M±m)

Region of kidney	Flight--weightlessness		Flight--centrifuge		Synchronous experiment	
	day of study					
	1	28	1	25	1	25
			H_2O (kg/kg dry substance)			
Cortex	3,1±0,1		2,96±0,09		2,8±0,06	
Medullary substance (external zone)	4,28±0,3		3,96±0,05		3,54±0,11	
Papilla (internal zone)	5,95±0,34		5,94±0,19		5,5±0,25	
			Na (meq/kg wet substance)			
Cortex	65,4±2,2	72,4±8,7	65,2±2,5	55,4±5,5	59,2±2,9	63,8±1,9
Medullary substance (extern.)	102,6±5,8	76,9±5,1	113,7±4,8	81,8±5,3	72,4±2,6	86,5±4,9
Papilla (intern.)	124,8±6,8	96,1±8,2	156,8±6,0	88,9±6,4	125,4±12,0	99,2±4,0
			Na (meq/kg dry substance)			
Cortex	267,5±7,4		260,6±14,9		225,8±12,5	
Medullary substance (extern.)	538,0±30,3		573,2±20,9		329,0±15,4	
Papilla (intern.)	884,2±40,0		1091,2±58,6		752,6±38,9	
			K (meq/kg wet substance)			
Cortex	70,6±1,0	74,6±2,5	78,1±1,8	77,2±2,2	79,2±0,2	73,3±1,9
Medullary substance (extern.)	63,6±3,3	68,0±1,4	68,9±2,6	70,9±2,6	76,6±0,95	74,6±6,1
Papilla (intern.)	58,6±5,4	66,8±4,3	71,9±2,9	60,3±1,2	81,5±3,0	65,4±2,3
			K (meq/kg dry substance)			
Cortex	289,8±10,7		310,8±4,2		300,6±4,2	
Medullary subst. (external)	332,0±9,3		346,7±15,2		347,8±5,5	
Papilla (intern.)	450,0±48,0		494,7±34,0		532,6±32,7	

Analysis revealed that the cause of decrease in concentration of potassium in different parts of the kidney is increased hydration of renal tissue, since potassium content did not change when scaled to dry substance (see Table). The change in cellular potassium concentration could be one of the causes of increased natriuresis in rats during the period of the water load, since a shortage of potassium diminishes reabsorption of sodium by cells of the thick ascending limb of Henle's loop [8].

The main finding of prior studies of fluid-electrolyte metabolism in experiments aboard Cosmos biosatellites was that there was a lower percentage of water input excreted by the kidney than after the synchronous experiment, while sodium and potassium balance was positive [4, 6]. The results of that study warrant the belief that the lower percentage of fluid excreted by the kidney on the 1st postflight day, in relation to fluid intake, is not related to fluid retention in the organism, but to a different level of extrarenal loss. Perhpas, this is due to increased expenditure of fluid in the postflight period by the rats to lick their coats, which was difficult to do when they were kept in the automated life support systems and under weightless conditions [6].

A comparison of the reaction of the human kidneys to a water load after a space flight and with simulation of weightlessness (prolonged hypodynamia with bed rest in antiorthostatic [head down] position) shows that there is fluid retention in both cases [1, 3]. The cause of differences in reactions to a water load of man and animals on the first day of the readaptation period is that there is very marked redistribution of fluid in man, because of his vertical body position, after he returns to his usual surroundings, and this is one of the important factors in fluid retention. In view of the horizontal position of great vessels in rats, such a reaction is not observed. The decreased fluid output after a water load in animals participating in the flight, on the 4th postflight day is apparently related to maximum retention of electrolytes at this stage of the study. Thus, maximum retention of sodium, potassium and calcium was noted on the 4th-5th day after the experiment aboard Cosmos-605 and on the 3d day of readaptation after the one aboard Cosmos-782.

Hypokalemia and a negative potassium balance develop in man when he remains in antiorthostatic position (simulation of weightlessness) for a long time. Under such conditions, the potassium load is eliminated faster, in spite of the potassium deficiency [7]. Such a phenomenon was also observed in rats after termination of the space flight experiment. These data indicate that a potassium load can be used to evaluate the body's ability to deposit potassium. With decrease in capacity of the depot (perhaps due to atrophy of muscle cells), potassium excretion increases, and this is demonstrable after the flight.

Thus, the greatest changes in fluid-electrolyte metabolism and ion-regulating function of the kidneys after the experiment aboard Cosmos-936 were noted in rats that were weightless during the flight. After a water load on the first day of readaptation, these animals presented increased sodium excretion. With a potassium load on the 2d postflight day, potassium excretion was at a maximum also in rats that had been submitted to weightlessness. Analysis of electrolyte composition of different parts of the kidney revealed a decrease in potassium content of wet cortical substance and medullary substance of the kidney, which is apparently due to increased tissular hydration. Microdissection of the kidney failed to demonstrate structural differences in nephrons of animals in different groups.

BIBLIOGRAPHY

1. Natochin, Yu. V.; Kozyrevskaya, G. I.; and Grigoryev, A. I. ACTA ASTRONAUT., Vol 2, 1975, pp 175-188.

2. Whedon, D.; Lutwaki, L.; Reid, I.; et al. Ibid, pp 297-309.

3. Grigor'yev, A. I.; Kozyrevskaya, G. I.; Natochin, Yu. V.; et al. in "Kosmicheskiye polety na korablyakh 'Soyuz'" [Space Flights Aboard the Soyuz Series Craft], Moscow, 1976, pp 226-234.

4. Ilyushko, N. A.; Il'in, Ye. A.; Kondrat'yev, Yu. I.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1977, pp 23-26.

5. Ilyushko, N. A.; Il'in, Ye. A.; Korol'kov, V. I.; et al. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, Vol 1, 1975, pp 12-14.

6. Ilyushko, N. A., and Kondrat'yev, Yu. I. "Trudy 8-kh chteniy, posvyashch. razrabotke nauchnogo naslediya i razvitiyu idey K. E. Tsiolkovskogo. Sektsiya 'Problemy kosmicheskoy meditsiny i biologii'" [Transactions of 8th Lectures Dedicated to Development of the Scientific Legacy and Ideas of K. E. Tsiolkovskiy. Section on "Problems of Space Medicine and Biology"], Moscow, 1974, pp 96-106.

7. Grigor'yev, A. I.; Dorokhova, B. R.; Kozyrevskaya, G. I.; et al. FIZIOLOGIYA CHELOVEKA [Human Physiology], No 4, 1979, pp 660-669.

8. Maxwell, M., and Kleeman, C. R. (editors) "Clinical Disorders of Fluid and Electrolyte Metabolism," New York, 1972, p 638.

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ACTIVITY OF SOME HEPATIC ENZYMES AND LIPOGENETIC PROCESSES IN RAT ADIPOSE TISSUE AFTER SPACE FLIGHT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 26-29

[Article by L. Makho, Sh. Nemet, M. Palkovich, V. Shtrbak and R. A. Tigranyan, submitted 17 Aug 78]

[English abstract from source]

The rats flown aboard Cosmos-782 showed a significant increase in the activity of tyrosine aminotransferase and tryptophan pyrolase, i. e. the enzymes whose activity depends on the corticosterone level. The synchronous rats displayed a small increase in the enzyme activity. The flight and synchronous animals exhibited a slight increase in the activity of gluconeogenetic enzymes and a decrease in the activity of glucose-6-phosphatase. Immediately after flight and, to a lesser extent, after the synchronous experiment the activity of lipogenetic enzymes decreased. On the R+25 day the enzyme activity remained unchanged. The study of lipogenesis in the epididymal fat, using C^{14}-glucose incorporation into lipids, did not reveal any differences in the flight and synchronous rats. The findings demonstrated that changes in the enzyme activity induced by the flight and synchronous experiments returned to the normal during readaptation.

[Text] Studies conducted in experiments aboard the Cosmos series of biosatellites revealed that prolonged weightlessness of rats leads to changes in some physiological functions, morphological state of organs and impairment of metabolic processes [1-6]. Morphological signs were demonstrated of increased functional activity of the hypothalamo-hypophyseo-adrenal system (HHAS) [1] and increased corticosterone concentration in blood plasma [5], which are indicative of a stress state due to the space flight factors. The space flight led to weight loss of the animals and decrease in adipose tissue in the subcutaneous fat and fat depots [3].

Our objective was to study the activity of some enzymes of the liver as related to corticosterone level in plasma, as well as enzymes of lipogenesis in the liver and processes of lipogenesis in adipose tissues of rats following a space flight.

Methods

The studies were conducted on male Wistar SPF rats 6-10 h and 26 days after a 19.5-day experiment aboard Cosmos-782. The obtained data were compared to the results of studies of animals in a synchronous experiment and vivarium control. To determine enzyme activity, liver specimens from animals sacrificed right after the flight were immediately frozen in liquid nitrogen and transported to the laboratory in a frozen state. Tissue homogenates were analyzed for activity of the following: tyrosine aminotransferase (TAT) [7], tryptophan pyrrolase (TP) [8], alanine aminotransferase (ALT) and asparate aminotransferase (AST; by the Farb Test method, Boeringer, Mannheim), phosphoenopyruvate carboxykinase (PEPCK) [9], fructose diphosphatase (FDP) [10], glucose-6-phosphatase (G6P) [11], malic enzyme [malate dehydrogenase] (ME) [12], glycerol phosphate oxidase (GP) [13], ATP citrate lyase [14] and serine dehydrase (SD) [15]. Protein was assayed by the method of Lowry et al. [16]. After the readaptation period (i.e., 26th day after landing), determination was also made of radioactive carbon-labeled glucose uptake in lipids of adipose (epididymal) tissue [17] and in the lipid fraction after separation by thin-layer chromatography [17].

Results and Discussion

Figures 1 and 2 illustrate data on activity of enzymes of amino acid metabolism in the liver of control and flight animals. A significant increase in TAT and TP activity was demonstrated in rats involved in the 19.5 day flight and sacrificed 6-10 h after termination thereof. The activity of these hepatic enzymes is very dependent on adrenocortical hormone level, and it increases already after one injection of corticosterone [18, 19]. Some increase in activity of both hepatic enzymes was demonstrated in rats used in the synchronous experiment.

TP activity in the liver of rats used in the flight and synchronous experiments 26 days after the flight did not differ from its activity in the control group, whereas TAT activity was lower in flight animals than the control. In the second half of the experiment, control animals presented high TAT activity in the liver.

Determination of ALT, AST and SD activity revealed that, immediately after the flight, AST activity was higher than in rats of both control groups; ALT and SD activity after the flight and synchronous experiments showed virtually no difference from that of animals in the vivarium control (see Figures 1 and 2).

After lengthy weightlessness, we observed only a minor increase in FDP and PEPCK activity (see Figure 2); FDP activity was also higher in the synchronous experiment. In the first hours after the flight and synchronous experiment there was a decrease in G6P activity; however, during the readaptation period, the activity of this gluconeogenetic enzyme increased reliably in both groups of animals, as compared to control levels (see Figure 2).

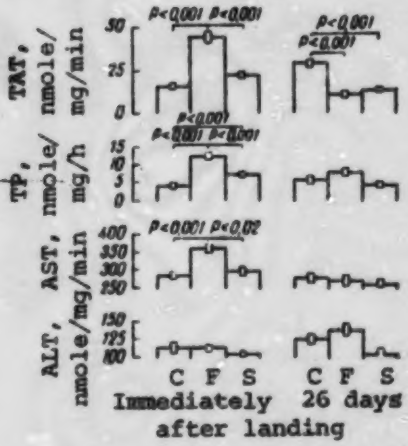

Figure 1.
TAT, TP, AST and ALT activity in rat liver. Here and in Figure 2:
C) control
F) flight
S) synchronous experiment

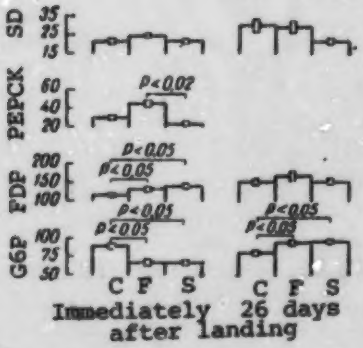

Figure 2.
SD, PEPCK, FDP and G6P activity in rat liver (nmole/mg/min)

The obtained results warrant the conclusion that there is an increase in processes of gluconeogenesis in animals used in the flight and synchronous experiments. The decrease in G6P activity in the first hours after the flight indicates that the glucose synthesized in the process of gluconeogenesis is utilized mainly for glycogen synthesis in the liver; but, in view of increased activity by the end of the readaptation period, G6P is released in a free form into the blood. There was significant increase in blood glucose concentration in rats sacrificed 6-10 h after the flight [5].

The concurrent increase in plasma corticosterone concentration after the flight [5] and elevation of blood glucose level are the result of inhibited utilization thereof, as was shown in other models of stress [20].

Determination of ME and ATP citrate lyase activity in the liver showed that it was significantly decreased immediately after the flight and in animals of the synchronous ground-based experiment. ME activity did not differ from the control 26 days after the flight and synchronous experiment (Figure 3). The obtained results indicate that keeping rats in the box-cages aboard the biosatellite and in the mock-up has an inhibitory effect on processes of biosynthesis of fatty acids. After the readaptation period, there is probable normalisation of hepatic lipid biosynthesis. The change in ME activity is unrelated to the influence of thyroid hormones, since GP activity does not change after the flight, and this enzyme is very sensitive to thyroxine [13].

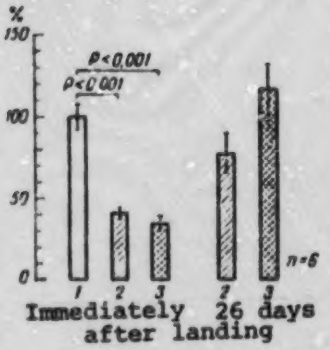

Figure 3.
ME activity in rat liver (% of control). Here and in Figure 4:
1) vivarium control
2) synchronous ground-based experiment
3) flight

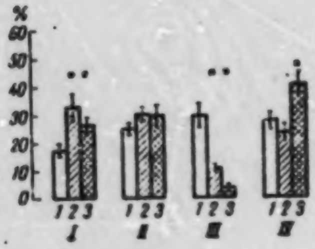

Figure 4.
Glucose uptake in adipose tissue lipid fraction
I) "start" fraction
II) mono- and diglycerides
III) fatty acids
IV) triglycerides
*) $P<0.01$, as compared to control

After readaptation to earth's gravity, flight animals failed to demonstrate reliable differences in rate of lipid biosynthesis in adipose tissue. However, separation of lipids into fractions (Figure 4) revealed that, in flight rats, there is significant uptake of glucose in the triglyceride and "start" fractions (probably, polar lipids, phospholipids), as a result of which there is a decrease in fatty acid fraction.

A comparison of the results of determination of activity of enzymes of amino acid metabolism and gluconeogenesis in the rat liver after the flight, as well as with acute and recurrent stress [18, 19], revealed that experimental animals presented an increase primarily in activity of enzymes (PEPCK, TAT, TP), the amount of which increased already after a single injection of corticosterone [18]. However, the activity of enzymes, the amount of which in the liver increases only after repeated injection of corticosteroids or after repeated stress [19], did not differ in animals after the space flight and ground-based synchronous experiment, as compared to control levels.

The obtained data indicate that the increase in activity of the HHAS and hepatic enzymes is primarily the result of the effects of the set of factors of acute stress during the final stage of the experiment, while prolonged weightlessness does not induce the same changes as repeated stress does in activity of hepatic enzymes [18, 19]. There was a decrease in activity of lipogenetic enzymes of the liver and fatty acid synthesis in weightless rats and those of the synchronous experiment. In spite of this, the rats in the flight and synchronous experiment groups presented an increase in concentration of triglycerides in the liver and nonesterified fatty acids in plasma and adipose tissue [6]. It may be assumed that increased lipid mobilization in adipose tissue is the cause of increase in nonesterified fatty acids and triglycerides of the liver, although processes of lipogenesis were diminished in this organ. By the end of the readaptation period, the indices of activity of lipogenetic enzymes of the liver were essentially restored to normal. Uptake of glucose in total lipids of experimental animals also failed to differ from the intact control; however, after completion of the flight, there was increase in incorporation of glucose in triglycerides and the fraction with phospholipids in adipose tissue. It may be assumed that glucose is incorporated in these molecules of lipid fractions chiefly in the form of glycerol. In the future, it will be necessary to pay attention to these changes in lipid metabolism of adipose tissue of animals used in space flights and ground-based model experiments.

BIBLIOGRAPHY

1. Portugalov, V. V.; Savina, Ye. A.; Kaplanskiy, A. S.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1976, pp 19-25.

2. Gazenko, O. G.; Demin, N. N.; Panev, A. N.; et al. Ibid, pp 14-19.

3. Il'in, Ye. A.; Serova, L. V.; and Noskin, A. D. Ibid, No 3, pp 9-14.

4. Gayevskaya, M. S.; Ushakov, A. S.; Belitskaya, R. A.; et al. Ibid, No 4, pp 25-30.

5. Tigranyan, R. A.; Popova, I. A.; et al. in "Simpozium po kosmicheskoy biologii i meditsine. 9-y. Tezisy dokladov" [Summaries of Papers Delivered at the 9th Symposium on Space Biology and Medicine], Budapest, 1976, p 83.

6. Alers, I.; Tigranyan, R. A.; et al. Ibid, p 96.

7. Diamondstone, T. L. ANALYT. BIOCHEM., Vol 16, 1966, pp 395-401.

8. Knox, W. E., and Auerbach, V. H. J. BIOL. CHEM., Vol 214, 1955, pp 307-313.

9. Nordlie, R. C., and Lardy, H. A. Ibid, Vol 238, 1963, pp 2259-2263.

10. Taketa, K., and Pogell, B. M. Ibid, Vol 240, 1965, pp 651-662.

11. Harper, A. E., and Bergmayer, M. W. in "Methods of Chemical Analysis," Weinheim, 1962, p 788.

12. Ballard, F. J., and Hanson, R. W. BIOCHEM. J., Vol 102, 1967, pp 952-958.

13. Hemon, P. BIOCHIM. BIOPHYS. ACTA, Vol 132, 1967, pp 175-178.

14. Srere, P. A. J. BIOL. CHEM., Vol 234, 1959, pp 2544-2547.

15. Goldstein, L., Knox, W. E.; et al. Ibid, V-1 237, 1962, pp 2855-2860.

16. Lowry, O. H.; Rosebrough, N. J.; Farr, A. L.; et al. Ibid, Vol 193, 1951, pp 265-275.

17. Macho, L., and Saffran, M. ENDOCRINOLOGY, Vol 81, 1967, pp 179-185.

18. Nemeth, S. LEK. OBZ., Vol 23, 1974, pp 359-363.

19. Idem, in "Hormones, Metabolism and Stress," Bratislava, 1973, pp 229-241.

20. Nemeth, S., and Vigas, M. ENDOCR. EXP., Vol 2, 1968, pp 179-184.

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STATE OF RAT THYROID C CELLS FOLLOWING FLIGHTS ON THE COSMOS TYPE OF BIOSATELLITES (ACCORDING TO RESULTS OF A MORPHOLOGICAL STUDY)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 29-33

[Article by G. I. Plakhuta-Plakutina, submitted 28 Jan 79]

[English abstract from source]

Calcitonin-secreting cells (C-cells) of the thyroid glands from 51 SPF Wistar rats flown for 18.5 to 22 days aboard biosatellites Cosmos-605, 782 and 936 and sacrificed 4.5—13 hours, 1—2 and 25—27 days after recovery were examined histologically and karyometrically. Vivarium (57) and synchronous (58) rats were used as controls. Variations in the nuclear volume of C-cells and their density were shown to depend on the experimental conditions and time interval elapsed after recovery. Morphological changes in C-cells were assumed to be associated with alterations in calcium metabolism during an exposure of rats to weightlessness, artificial gravity and Earth gravity.

[Text] According to data in the literature, the hormone thyrocalcitonin secreted by thyroid C cells has a hypocalcemic action, which is the opposite of the action of parathyroid hormone, due to inhibition of resorptive processes in bone tissue [1-4], while an increase in number and size of C cell nuclei is indicative of increased calcitonin synthesis [5-8].

Previous studies of the rat thyroid after a flight aboard the Cosmos-605 biosatellite established a significant increase in calcitonin-secreting cells and morphological signs of increased functional activity thereof [9]. However, it was not possible to determine whether this phenomenon is related to space flight factors (in particular, weightlessness or the period of return to earth's gravity), since the animals were sacrificed 1-2 days after the flight, and the changes in both C cells and the thyroid proper could have been due to gravitational stress.

Since animals were sacrificed as soon as feasible after termination of the flights aboard Cosmos-782 and Cosmos-936, we were able to compare the results of histological and karyometric studies of thyroid C cells within the first 4.5-13 h and 2 days after long-term weightlessness.

Methods

The material studied consisted of thyroids from 15 male Wistar rats that had been aboard Cosmos-605 for a 22-day flight and 11 Wistar SPF rats that had spent 19.5 days aboard Cosmos-782. The distinctive element of the experiment conducted aboard Cosmos-936 was that artificial gravity simulating earth's gravity was created [10]. The thyroids of 15 rats that had spent 18.5 days in weightlessness and 10 kept on a centrifuge during the flight were submitted to examination. As a control for each of these flight experiments, we used an equal number of rats from ground-based model experiments, in which all space flight factors were simulated with the exception of weightlessness, as well as intact animals that remained in the vivarium throughout the experiment. The animals were decapitated 4.5-13 h and 1-2 days after the flight and termination of ground-based experiments, as well as after 25-27 days of the aftereffect period.

The excised thyroid (from a total of 166 rats) was fixed in Bouin fluid and imbedded in paraffin. The sections were stained with hematoxylin and eosin, as well as Heidenhain's azan. The colloid in the thyroid was stained according to Marais and Ham [11]. We used hematoxylin and luminous green, and impregnation with silver nitrate by the method of Grandi [12] to demonstrate C cells and assess their functional state.

C cells were counted using an ocular grid at magnifications of 40× for the objective and 7× for the ocular. C cell nucleus volume was measured using an RA-6 projection attachment [drafting machine] (MBI-11 microscope). At a linear magnification of 2000×, we drew the outline projections of 100 C cell nuclei from sections of thyroid from each animal, and determined the logarithms of their volumes using the formula for an ellipsoid of revolution [spheroid]:

$$V = \frac{\pi}{6} (LD)^{3/2}$$

and the nomograms of Fischer and Inke [13]. Subsequent calculations were made by the conventional karyometric methods of variational statistics [14]. The results were considered reliable with $P<0.05$. The reliability of differences was determined by the criterion of Student and Fisher.

Results and Discussion

A reliable decrease in number of C cells (by 18%) was demonstrated in rats taken from Cosmos-936, which had been weightless during the flight and were sacrificed within 4.5-9 h after the flight, as compared to the vivarium control ($P<0.01$).

The C cells presented mainly epifollicular localization, and they were not always clearly circumscribed with use of the ordinary staining methods. Impregnation of sections according to Grandi revealed that the C cells were small, more often encountered alone and they seldom formed accumulations. With regard to secretory granule content, they were very similar: the granules were dark, fine and arranged in the form of narrow bands in the perinuclear region of the cytoplasm in most cells.

Karyometric studies revealed a substantial decrease in volume of C cell nuclei in flight group rats: by 32.6% as compared to the vivarium control (99.5±6.1 and 147.6 3.3 μm^3, respectively, $P<0.001$). The variational curve of logarithms of the volume of C cell nuclei was distinctly shifted to the left for rats in the weightless group, which was indicative of prevalence of small nuclei (Figure 1).

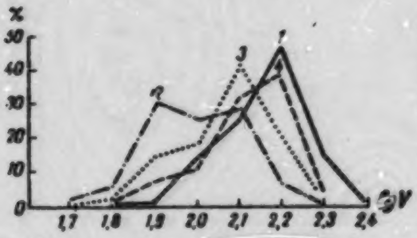

Figure 1.
Variational curves of logarithms of volume of thyroid C cell nuclei (Cosmos-936). X-axis, classes of nucleus volume (logarithms); y-axis, % nuclei in each class. Here and in Figure 2:

1) vivarium control
2) weightlessness
3) ground-based synchronous experiment
4) artificial gravity in flight

There was an increase in number of demonstrable parafollicular cells 9-11 h after flight (Cosmos-782), and the number was close to the control ($P \leq 0.05$), whereas the size of C cell nuclei did not yet reach control values (Figure 2).

Examination of thyroid tissue within 4.5-13 h after the flight revealed morphological signs of some decrease in function, as manifested by a decrease in height of follicular epithelium, consolidation of colloid and absence of resorption vacuoles. In addition, there was prevalence of follicles with yellow colloid, indicative of decrease in iodinated amino acid content of the colloid.

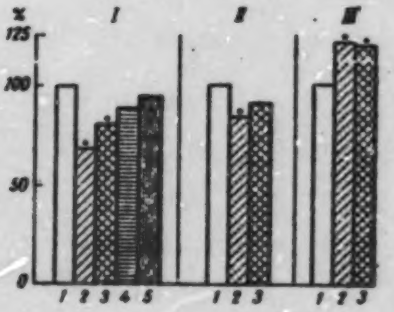

Figure 2.
Dynamics of changes in thyroid C cell nucleus volume. Vertical axis, C cell nucleus volume (% of control). The dots refer to reliable differences from control

I) Cosmos-936 (4.5-9 h after land-landing)
II) Cosmos-782 (9-11 h after land.)
III) Cosmos-605 (48 h. " "
5) animals rotated in ground-based centrifuge at 1.4 G

We demonstrated a decrease in size of C cell nuclei (118.6±2.3 μm^3), as is clearly seen in Figure 1, in rats from the ground-based experiment, which simulated flight conditions, as in animals submitted to weightlessness. The similar direction of changes in C cells in the compared groups warrants the belief that the decrease in number of C cells and morphological signs of depressed function thereof are related to the influence of weightlessness and hypokinesia.

In rats kept on a centrifuge during the flight, the histology of the thyroid differed from that of rats in the weightless group in that there were signs indicative of some increase in functional activity. The follicular epithelium was tall, cuboidal, and colloid was less dense than in rats submitted to weightlessness, often with fine marginal vacuoles; its tinctorial properties did not differ from those of colloid of intact animals. Interfollicular tissue was represented by proliferative islets, among which parafollicular cells were often encountered. The latter, according to degree of cytoplasmic granulation, were at different stages of the secretory cycle. The population of C cells of rats put on the centrifuge was considerably larger than in the group of rats submitted to weightlessness (by 37%; $P<0.001$), but close to the population size in animals from the vivarium control ($P<0.05$). The C cell nucleus volume constituted 131.3±6.3 μm^3, and it did not differ from the control with statistical reliability (see Figures 1 and 2).

In rats from Cosmos-605 examined 48 h after the flight, we found morphological signs of activation of the thyroid, manifested by capillary plethora, epithelial polymorphism, clearing and vacuolization of apical ends of the thyrocytes, liquefaction and resorption of colloid. Visual examination of preparations revealed impressive increase in number and size of C cells, which were encountered chiefly in the central parts of the gland, isolated in the walls of follicles or in groups of 4-6 cells in interfollicular tissue. A count of the C cells revealed a significant increase in their number (by 92.3%) and nuclear volume (by 22%); we also observed varying degrees of cytoplasmic degranulation on sections impregnated by the Grandi method more often than in control animals.

The histological structure of the thyroid of rats in the flight group did not differ from that of animals from the corresponding ground experiments and vivarium control 25-27 days after completion of the flight. The morphological features of the C cells also failed to demonstrate differences from the control, but their number remained high and was 13% above the control level.

Analysis of morphometric data for C cells of animals flown aboard the biosatellites and sacrificed at different times after the flights revealed that the transition from weightlessness to earth's gravity is a powerful stimulus for activation of the C cell system. Indeed, it was logical to expect a reaction from the calcitonin-secreting cells, the hormone of which, as we know, reduces elimination of calcium from bones and inhibits resorption of the bone matrix [15, 16], while morphological signs of functional changes are manifested quite rapidly, within a few hours to 1 day [17-19].

Within the first few hours after the flight, there was a decrease in number and size of C cells, with signs of decreased functional activity, against the background of some signs of hypofunction, which were also noted in the gland's parenchyma, which is apparently a reflection of the morphofunctional state of the thyroid during the period of weightlessness.

The use of artificial gravity eliminated the changes induced by weightlessness, since the number of C cells, the volume of their nuclei and degree of granulation of cytoplasm, as well as general structure of the gland itself, virtually failed to differ from the findings on rats in the vivarium control. The subsequent dynamics of increase in number and volume of C cell nuclei, particularly marked 48 h after the flight, lead us to evaluate this as an expression of an adaptive reaction directed toward increasing the release of thyrocalcitonin to stabilize calcium of bone tissue when the animals returned to earth's gravity, i.e., as an immediate reaction to gravitational stress. This thesis is also confirmed by the calcium retention found in animals flown aboard the biosatellites, which was at a maximum on the 2d-5th and 11th-12th days of the readaptation period [20].

Thus, the submitted material indicates the following: 1) absence of gravity during a long space flight leads to a decrease in functional activity of thyroid C cells in rats; on this basis, it may be assumed that, in weightlessness, C cells "do not hinder" free release of calcium ions from bone tissue; 2) exposure of animals aboard the biosatellite to artificial gravity helps preserve the morphological and functional distinctions of C cells and the thyroid itself, which are inherent in ground-based conditions; the latter warrants the belief that artificial gravity, which simulates earth's gravity, prevents changes in the thyroid that are related to weightlessness; 3) intensification of functional activity of C cells in the postflight period is a reaction to the transition from weightlessness to earth's gravity. This reaction develops in time, and it is directed toward stabilizing calcium in osseous tissue.

BIBLIOGRAPHY

1. Briskin, A. I.; Odinokova, V. A.; Kondalenko, V. F.; et al. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 2, 1971, pp 111-113.

2. Briskin, A. I.; Volozhin, A. I.; and Shashkov, V. S. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1976, pp 17-22.

3. Hirsh, O. F., and Munson, P. L. PHYSIOL. REV., Vol 49, 1969, pp 548-622.

4. Baylink, D.; Morey, E.; and Rich, C. ENDOCRINOLOGY, Vol 84, 1969, pp 261-269.

5. Kameda, J. ARCH. HISTOL. JAP., Vol 32, 1970, pp 179-192.

6. Lietz, H. VIRCHOW'S ARCH., Abt. A: "Path. Anat.," Vol 350, 1970, pp 136-149.

7. Stachura, J., and Pearse, A. G. Ibid, Pt. B: "Zellpath.," Vol 5, 1970, pp 173-186.

8. Mietkivski, K.; Lukaszyk, A.; and Zabel, M. ENDOKR. POL., Vol 24, 1973, pp 57-70.

9. Plakhuta-Plakutina, G. I. in "Simpozium po kosmicheskoy biologii i meditsine. 10-y. Tezisy" [Summaries of Papers Delivered at 10th Symposium on Space Biology and Medicine], Moscow, 1977, pp 53-54.

10. Il'in, Ye. A.; Korol'kov, V. I.; Kotovskaya, A. R.; et al. KOSMICHESKAYA BIOL,, No 6, 1979, pp 18-22.

11. Marais, A., and LaHam, V. N. CANAD. J. BIOCHEM., Vol 40, 1962, pp 227-238.

12. Grandi, P. VIRCHOW'S ARCH., Pt. B: "Zellpath., Vol 6, 1970, pp 137-150.

13. Fischer, J., and Inke, G. ACTA MORPH. ACAD. SCI. HUNG., Vol 7, 1956, pp 141-165.

14. Khesin, Ya. Ye. "Size of Nuclei and Functional State of Cells," Moscow, 1967, pp 10-33.

15. Khomullo, G. V. (editor) "Thyrocalcitonin and Repair Regeneration of Tissues Under Experimental and Clinical Conditions," Moscow, 1974.

16. Prokhonchukov, A. A.; Khomullo, G. V.; Briskin, A. I.; et al. PROBL. ENDOKRINOL. [Problems of Endocrinology], No 6, 1974, pp 80-85.

17. Matsuzawa, T., and Kurosumi, K. NATURE, Vol 213, 1967, pp 927-928.

18. Hachmeister, U.; Bonicke, J.; Lenke, M.; et al. in "Testosterone. Struma," Berlin, 1968, pp 268-271.

19. Zabel, M., and Peil, J. in "Annual of Morphology and Microscopic Anatomy," Leipzig, Pt 1, Vol 120, No 6, 1974, pp 854-861.

20. Ilyushko, N. A., and Kondrat'yev, Yu. I. in "Simpozium po kosmicheskoy biologii i meditsine. 10-y. Tezisy," Moscow, 1977, p 28.

UDC: 613.693-07:612.821

SOME ASPECTS OF APPLICATION OF THE SYSTEMIC APPROACH TO AVIATION ENGINEERING PSYCHOLOGY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 33-37

[Article by V. A. Ponomarenko and N. D. Zavalova, submitted 26 Mar 79]

[English abstract from source]

The paper shows the role of study and analysis of systemic properties of the equipment of cockpits for its optimization. The paper describes and classifies pilot's errors caused by disadvantages of the total systemic quality of various components of the equipment. The paper presents methods for eliminating causes of some erroneous actions of pilots.

[Text] The pilot-aircraft system was the subject of studies in human engineering in aviation. The properties of a system cannot be reduced to the sum of properties of its elements, since the latter interact with one another and their properties emerge in their correlations [1]. As applied to the pilot-aircraft system, this is manifested by the fact that the efficiency and reliability of the system is not determined by biological and psychological traits of the pilot considered separately or by the technical properties of equipment, but by the aggregate of properties of interaction between man and machine, which are demonstrable only in the process of control, when man uses machines.

The components of a system have a systemic [integral] quality, in addition to their inherent natural ones. A systemic quality refers to the property of a system component that is expressed through the integrative properties of the aggregate and integrity of the system [1]. For example, the reliability of actions is the systemic quality of the pilot as a component of the pilot-aircraft system, which can be demonstrated only when the pilot interacts with the aircraft.

Aviation psychology deals with a complex system, which includes as components both man and machine. Efforts to study the features of a pilot (his skills, ability, attention, memory, thinking, etc.) and technical characteristics (controllability and stability of the aircraft, information model, etc.) separately and then add up the obtained data failed to yield the desired result, i.e., to evaluation of tension and difficulty of pilot work, reliability and efficiency of his actions under different flying conditions. This occurs because separate studies of components do not and cannot make it possible to characterize systemic qualities.

We shall discuss the distinctions of a systemic quality on the example of evaluation of the quality of an ejection seat. If the latter is only considered as an ejection device, rating of its quality would be wrong, since the seat should provide for convenient manual and foot control, accessibility of all aircraft controls, possibility of adjusting seat height, as well as serve as a means of survival after ejection, i.e., in the pilot-aircraft system the rating of the seat should be different from a rating thereof solely as an ejection device. It would seem that this is a fact, yet in designing different types of cockpit equipment the multifunctionality of each component, its intrasystemic relations and dependence of quality on how the equipment will be used in the work process are often overlooked.

The use of the systemic approach is particularly important for solving the problem of flight safety. We shall deal with interaction between two components of the pilot-aircraft system: technical and psychological (human). The requirement of the technical component of the system is primarily that the aircraft equipment conform with the capabilities and properties of the man who controls the aircraft, or the quality of adjustment [fitting together] of the equipment to the pilot. In order to design an aircraft with the quality of fitting together, one must conduct scientific research directed toward assuring reliability of equipment, laboratory and bench tests for structural strength of the aircraft, flight tests of soundness and controllability of the aircraft in different flight conditions. Human engineering studies of the quality of interaction between the pilot and aircraft, including situations where there are malfunctions (studies of reliability of back-up equipment provided by man) are also important. It is expressly the adjustment of equipment to the pilot's properties that is a systemic quality of the technical component that aids in reliability of the pilot's provisions for malfunctioning equipment and, consequently, flight safety. The systemic quality of the psychological component is the efficiency and reliability of actions by the pilot controlling the aircraft. This systemic quality is obtained by means of special training for operation of specific equipment, for action in case of technical malfunction, purposefulness of the pilot with regard to performing the tasks, for which the pilot-aircraft system is designed, and, of course, adjustment of equipment to man.

The systemic qualities of the technical and human components--adjustment of equipment to man, efficiency and reliability of man's action--do not exist apart from one another and cannot be manifested outside the pilot-aircraft system. Of course, providing for safety cannot be achieved only by strengthening the technical component (refining instruments, automating control, etc.) without consideration of human properties or, on the contrary, only the human component (development of skills, life support, screening, setting labor standards, etc.) without consideration of the quality of aircraft equipment. The systemic approach to solving the safety problem is based on determination of correlations and interrelations between these two components.

Thus, the pilot and aircraft are united in a system which, like any system, consists of an aggregate of components that are coordinated to reach a common goal. The efficiency of the system is not so much a function of the components proper as of their interactions and interdependence. This means that neither a trained specialist nor refined equipment considered separately can guarantee the safety of a flight.

The cause of flight accidents is often related to human errors. In this regard, we shall discuss the possibility of using the systemic approach to the study of pilot errors. Heretofore, only the personal factor, i.e., psychological, physiological and other traits inherent in man as a concrete individual, was often mentioned in establishing that human error was the cause of a flight accident. We believe that use of the concept of "personal factor" is not sufficient to refer to pilot error as a cause. When reference is made to the personal factor, the process of interaction between man and equipment is disregarded, and without this it is impossible to establish the true cause of a flight accident [or incident]. The systemic approach to analysis of causes and errors made it necessary to introduce another concept, "the human factor,"* which contains the idea of dependence of characteristics of human actions on the properties of equipment. In this case, pilot error is an integral indicator of the shortcomings of interaction between man and equipment, adjustment of equipment to man.

The systemic approach made it possible to disclose a class of errors "built into equipment," embodied in it due to underestimation of human traits in designing it. These errors are not referable to man alone, they are manifested through interaction between the pilot and aircraft. The lack of a systemic approach to analysis of the causes of errors results in classification of errors built into equipment, when they are manifested, as errors of action by the fault of man. For example, there is the error of moving a control too far, which causes impairment of piloting conditions. This error is typical of control systems that are so designed that, in the event of increased acceleration [or overload], the pilot would reduce the muscular force applied to alter this. Such a control system requires fine differentiation between muscular exertions by the pilot in the presence of high accelerations, i.e., expressly under conditions when such differentiation is impossible. In this case, the condition is built into the equipment that provokes pilot error. In its design, due consideration was not given to the fact that the very presence of acceleration impairs subjective evaluation of the muscular force applied to the controls, and it is perceived as weaker.

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*The concept of "human factor" is in the realm of engineering psychology. However, in recent years, the words "personal factor" and "human factor" have been used as synonyms in investigations of flight accidents.

The systemic approach makes it possible to choose steps that aid in overcoming pilot error. It is directed toward demonstration of the genesis of erroneous action. For this purpose, one must examine integral activity. According to psychological theory [2], the activity meets certain demands of man and is characterized by a certain motive. Activity is performed through actions that are directed toward a concrete result and determined by consciously set goals. The action is performed through different operations, the composition of which is not related to the goal, but to the conditions under which the goal must be reached. Thus, a distinction is made between three levels in the macrostructure of activity: activity, action, operation.

An error may occur on each macrostructural level of activity. An error occurs on the first level as a result of distortion of the motive, the need of the man performing the activity. On the second level, it could result from inconsistency bewtween man's subjective goal and the objectively set task, the result of distortion of the conceptual model (image-goal) and paucity of operational images. On the third level, the error is related to inconsistency of conditions and tasks, and it is manifested by failure to perform certain movements, poor coordination, missing a signal, etc. While prevention of errors due to motivational flaws (first level) involves training of the pilot's personality, screening of individuals for flight work, to overcome errors of action requires consistency of the information model with the pilots need for information and training, an information model that would be adequate to the pilot's tasks. Overcoming errors on the third level requires the development of automated skills, optimization of arrangement of controls and indicator devices in the cabin, better design of the dials of the indicator devices.

Apparently, a distinction is made between internal mechanisms that are similar in manifestation of error and, consequently, the measures to overcome these errors, depending on the genesis of the error. Consideration of the cause of motor or other errors only as a deficiency referable to skill is tantamount to canceling them out, reducing them to the operational level (occurring on the third level). As a result, the impression is gained that it is very simple to eliminate the cause of errors. The corresponding measures are developed; however, they turn out to be ineffective. Use of the systemic approach, which implies understanding of pilot activity, which is not reduced to the sum of operations, indicates the complexity and multivalence of causes of errors. First of all, it takes into consideration the relation of the error to the goal of action, to characteristics of the image that regulates action. Only the systemic approach permits disclosure of the deep internal causes of pilot error. Systemic analysis shows that the origin of errors cannot be deduced from one source and reduced to one cause. Each specific error is caused by a multitude of causes.

Let us consider how different sources and causes of errors are interrelated in a pilot-aircraft system. Man, who has certain personality, professional and somatic distinctions, and equipment, which includes the features of the pilot's work place, information model, control systems and aircraft aerodynamics, are the chief causes of errors. Under actual flight conditions, the sources of errors are interrelated. There are two initial causes of errors: flaws referable to interaction between man and machine (human factor) and limited capabilities and shortcomings of the pilot (personal factor). The immediate causes of errors related to the human factor are incomplete, false and vague information, uncoordinated delivery of signals, poor design of indicator dials, low attention-attracting effect of signaling devices, inconvenient location of control levers, inconsistency of laws for control and human reactions, uncoordinated distribution of functions between man and automatic equipment, and many others. The immediate causes of errors related to the personal factor may be poor pilot training, inadequate motivation, unfavorable individual psychological distinctions, health-related flaws, etc. Errors, the cause of which are flaws in interaction between the pilot and aircraft, are aggravated under the influence of adverse flight factors, as well as an adverse personal factor. Favorable personality traits in the pilot, on the contrary, help avert part of the consistent errors built into the equipment or minimize their adverse consequences.

The material we have discussed helped demonstrate the complexity of such an ordinary factor, it would seem at first glance, as pilot error. Systemic analysis demonstrated the elements of its complexity: an error occurs due to flaws in the aggregate systemic quality of some component of the system, and its cause cannot be disclosed without consideration of the relations between components in the pilot-aircraft system.

Use of the systemic approach to the study of flight work makes it possible to derive some conclusions of practical importance: 1) psychological forecast of flight safety should be made on the basis of studying the integral pilot-aircraft system, studies of the characteristics of interaction between pilot and machine under different flying conditions; 2) improvement of efficiency and reliability of flight work should be made by providing for the systemic quality of the technical component, i.e., adjustment of equipment to man; 3) most often, pilot error is not related exclusively to the personal factor; for this reason, unilateral orientation of efforts toward education, training and medical supervision cannot assure a substantial decline in number of in-flight errors. To prevent errors, it is imperative to make a concrete analysis of all elements of interaction between the pilot and aircraft equipment, in order to prepare recommendations for directed training of flight personnel and planning pilot activity in the aspect of human engineering.

BIBLIOGRAPHY

1. Kyaz'min, V. P. VOPR. FILOSOFII [Problems of Philosophy], No 9, 1976, pp 81-94; No 10, pp 95-106.

2. Leont'yev, A. N. "Activity. Consciousness. Personality," Moscow, 1975.

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EFFECT OF PROLONGED $+G_z$ ACCELERATIONS ON HUMAN PERFORMANCE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 37-40

[Article by A. S. Barer, T. A. Sokolova, V. M. Tardov and Yu. P. Yashin submitted 26 Jul 79

[English abstract from source]

With an increase in acceleration value the accuracy of human performance decreases. This becomes very noticeable at $+G_z > 5$ g. In this situation work capacity can be raised by increasing an angle between the G_z vector and the long axis of the human body. Pilots need to be tested for acceleration tolerance before they are allowed to fly at $+G_z \geqslant 8$ g.

[Text] It is known that the extent of circulatory disturbance under the influence of acceleration (other conditions being equal) is determined by the magnitude of its component in the axis of the pilot's head--pelvis ($+G_{z1}$), which is related both to the magnitude of overall acceleration of the aircraft and the angle between the direction of its action and longitudinal body axis [1-4]. Obviously, as this angle increases, the height of the hydrostatic column of blood between the heart and peripheral blood vessels diminishes. As a result, there is less deposition of blood, improved venous return to the heart and delivery of blood to the brain which, in turn, leads to better human performance [fitness]

This means of improving fitness in the presence of accelerations has found wide use in the design of manned spacecraft, and it is beginning to be adopted in the aircraft industry [5, 6]. In this regard, reports have recently appeared in the press concerning the results of research on the performance of human operators under different conditions, and for this purpose diverse flight simulating devices were used, in particular centrifuges [5-13]. At the same time, the influence of high $+G_z$ inherent in aviation on specific operator activity of pilots has not yet been sufficiently studied.

We report here the results of a study of the effects of +Gz acceleration and relative increase in angle of its orientation in relation to the longitudinal axis of the body on pilot performance.

Methods

There were 13 men ranging in age from 22 to 39 years participating in the studies; they were deemed fit for flight work with regard to their physical condition and had undergone a complete course of training on "piloting." This study was conducted on a piloting complex, which included a centrifuge with 8-m arm and a computer (Figure 1).

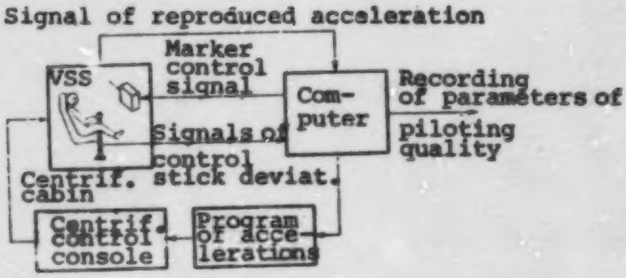
Signal of reproduced acceleration
Marker control signal
VSS
Computer
Recording of parameters of piloting quality
Signals of control stick deviat.
Centrif. cabin
Centrif. control console
Program of accelerations

Figure 1. Diagram of flight simulating complex

To evaluate operator performance, the test consisted of the task of tracking a moving marker light projected on the screen of a visual situation simulator (VSS). Deviations of the marker were compensated by means of a control stick [handle]. Signals proportionate to movement of the stick were transmitted from the centrifuge cabin to the computer, which solved equations of motion and controlled movement of the marker over the VSS screen to correspond to the task of piloting an aircraft.

The studies were conducted using different levels of accelerations at angles of 23 and 35° to the longitudinal axis of the human body, which enabled us to test performance as related both to the magnitude and direction of acceleration. The results were expressed in the form of parameters as functions of magnitude of the longitudinal component of acceleration, $+G_{z1}$, chosen as the general parameter for this series of studies.

In all, we conducted 207 tests with accelerations of 2, 4, 5, 6, 8 and 9 units.

Quality of performance was rated according to the mean square error of tracking σ. To evaluate distribution and range of attention, the subject checked the quality of his own performance: at times when in his opinion piloting accuracy was within the specified range he depressed a button. We took into consideration the number N of correct ratings of accuracy. In addition, to assess performance we also determined the maximum possible "piloting" time during exposure to 9 unit acceleration.

In all of the tests, we recorded the acceleration, EKG, systolic arterial pressure (AP) in vessels of the concha, photoplethysmogram (PPG) of the same region, minute volume of respiration (MV) reduced to the unified standard in the BTPS system.

In all cases, an anti-G suit was worn. In addition, to increase endurance of accelerations, we created tension of prelum abdominale and lower limb muscles.

The digital data obtained in the experiments were submitted to statistical processing using the system adopted in biomedical research.

Results and Discussion

These studies revealed that accelerations have a substantial effect on performance. Figure 2a illustrates the relative tracking error and relative decrease in number of correct self-evaluations of performance quality as a function of magnitude of the longitudinal component of acceleration G_{z1}. As can be seen in this figure, this dependence is particularly marked with accelerations in excess of 5 units, and there was the same degree of build-up in tracking errors and decrease in correct subjective rating of piloting quality up to $+G_{z1} \leq 7.5$ units. At higher acceleration levels, the number of correct subjecting ratings decreased much more than the increase in tracking error. Evidently, this phenomenon is related to the fact that the scope of operator attention under such conditions is virtually depleted, and he is unable to reliably perform any operation other than the main one (for example, "piloting").

The change in quality of "piloting" was quite consistent with the tested physiological parameters. Processing of physiological parameters and analysis of the subjects ratings enabled us to systematize the factors that limited endurance of accelerations and performance. The most frequent signs leading to loss of control or determining the range of endurance were found to be visual disorders, general fatigue and pain in the upper third of the forearm (ulnar surface), elbow and distal region of the arm.

As we know, visual disorders during exposure to accelerations are due to poorer circulation in the retina. We demonstrated a correlation between mean and lowest systolic AP in the "plateau"* in the region of the head

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*"Plateau" refers to the period of centrifuge rotation with a constant level of acceleration.

(sensor on the ear lobe), as well as amplitude of ear pulse, and the $+G_{z1}$ component of acceleration (Figure 2, b, c). As can be seen in this figure, the mean AP and ear pulse amplitude begin to decline appreciably with $+G_{z1}>4.5$ units. The minimum AP and ear pulse amplitude begin to decline at lower acceleration levels, and with $+G_{z1} = 6.5$ units they reach 30 mm Hg and 30% of initial amplitude, respectively, which is indicative of the possibility of visual disorders [14, 15].

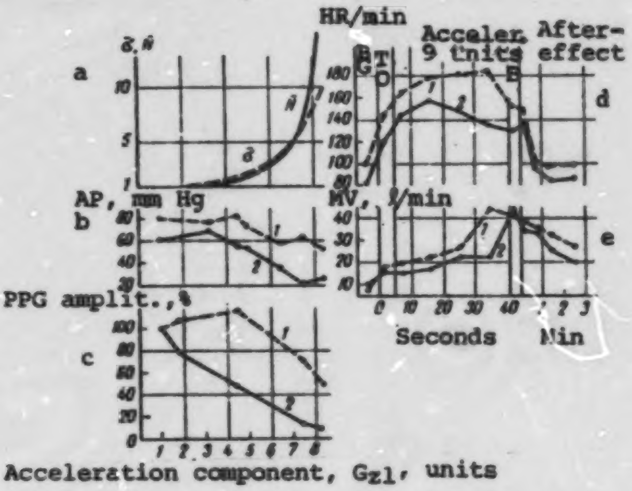


Figure 2. Changes in performance and some physiological parameters (statistical means) under the influence of different levels of acceleration

Key:

a) tracking error as related to base value ($\bar{\sigma} = \frac{\sigma \text{ with accelerations}}{\sigma \text{ in the initial state}}$), and degree of decrease in number N of correct subjective assessment of performance ($\bar{N} = \frac{N \text{ in the initial state}}{N \text{ with accelerations}}$)

b) mean (1) and minimum (2) systolic AP on "plateau"

c) mean (1) and minimum (2) amplitude of ear pulse on "plateau" (% of base values)

d,e) heart rate (HR) and MV in subjects with stable (1) and vagal (2) types of chronotropic cardiac reaction to 9-unit acceleration directed at an angle of 35° to the longitudinal axis of the body

BG) background

TO) take-off acceleration

B) braking

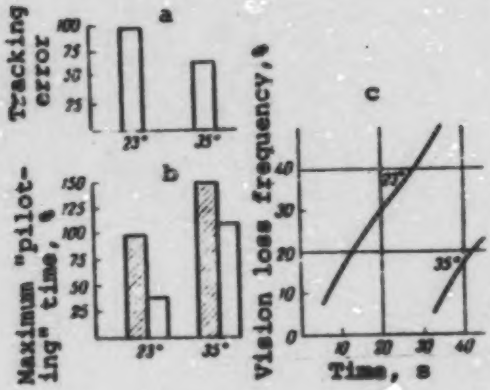


Figure 3.
Comparative evaluation of performance parameters (statistical means) with 9-unit acceleration at angles of 23 and 35° to longitudinal axis of the body

a) relative tracking error
b) correlation between maximum "piloting" times (striped columns, time for all subjects; white, for the group less tolerant to accelerations)
c) frequency of loss of vision (% of total number of tests) as a function of time

Fatigue, as a factor limiting performance with exposure to accelerations, is determined by the limited "energy resources" for compensation of functions and different systems of the body and maintenance of high muscular tension.

As for the pain in the arms with accelerations of the order of $+G_{z1}$ = 8.0÷8.5 units, they can be attributed to elevation of hydrostatic pressure and increased delivery of blood to vessels of the areas involved.

Very typical changes were observed under the influence of accelerations in dynamics of heart rate (HR) and pulmonary ventilation. Thus, starting at about the 15th s of accelerations of 9 units, there was distinct demonstration of two types of chronotropic cardiac reaction, stable and vagal [16], and they corresponded to different dynamics of changes in MV (Figure 2d). It is important to note that appearance of relative bradycardia was not associated with either decreased endurance or diminished performance.

This study also revealed that, among individuals who had undergone medical examination for determination of fitness for flying with positive results, there was rather clear distinction of a group of subjects with relatively poorer endurance of accelerations. Thus for the less resistant group of subjects, maximum piloting time at $+G_{z1}$ = 8.3 units was one-fourth the time for the others. The latter circumstance convinces us of the desirability of examining pilots for endurance and performance at Gz accelerations, and this is consistent with the recommendations of a number of other researchers [12, 17].

The results revealed that maximum "piloting time" at 9 units of acceleration increases (by a mean of 1.5 times) while tracking error decreases (to the same extent) when the angle between the vector of acceleration and longitudinal axis of the human body is increased from 23 to 35° (Figure 3, a, b). And for the group of less tolerant subjects, the increase in maximum "piloting" time is even greater (by 3 times; see Figure 3b).

Finally, it is important to mention that an increase in angle of tilt of the seat provides better compensation of circulation in the region of the head and, consequently, lowers appreciably the frequency and severity of visual disorders that limit the time of retention of fitness for work (Figure 3c).

BIBLIOGRAPHY

1. Barer, A. S.; Golov, G. A.; Zubavin, V. B.; et al. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow, Coll 1, 1967, pp 30-42.

2. Gell, C. F., and Hunter, N. N. J. AVIAT. MED., Vol 25, 1954, pp 568-577.

3. Kotovskaya, A. R.; Vasil'yev, P. V.; Lapin, B. A.; et al. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 4, 1965, pp 322-332.

4. Sergeyev, A. A. "Physiological Mechanisms of Effects of Accelerations," Leningrad, 1967.

5. Burton, R. R.; Japietro, P. F.; and Leverett, S. D. AVIAT. SPACE ENVIRONM. MED., Vol 46, 1975, pp 887-897.

6. "Special Report F-16 Multinational Fighter Program," AVIAT. WEEK SPACE TECHNOL., Vol 106, No 18, 1977, pp 44-130.

7. Prilliman, F. W. Nuff, W. W., Jr.; and Hooks, J. T., Jr. J. AIRCRAFT, Vol 6, 1969, pp 353-359.

8. Acklat, D. J. AIRCRAFT ENG., Vol 44, 1972, pp 4-8.

9. Volkov, A. A.: Denisov, V. G.; Kirilenko, Yu. I.; et al. in "Sistema 'Chelovek i avtomat'" [Man-Machine Systems], Moscow, 1965, pp 215-228.

10. Kakurin, L. I.; Kotovskaya, A. R.; Filosofov, V. K.; et al. Ibid, pp 241-244.

11. Zorile, V. I., and Kupriyanov, A. A. VOYEN.-MED. ZH. [Military Medical Journal], No 6, 1972, pp 89-94.

12. Barer, A. S.; Yeliseyev, A. S.; Panfilov, V. Ye.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 1, 1968, pp 54-57.

13. Kotovskaya, A. R.; Vartbaronov, R. A.; and Khomenko, M. N. Ibid, No 6, 1977, pp 12-19.

14. Kotovskaya, A. R.: Vartbaronov, R. A.; and Nikol'skiy, L. N. Ibid, No 1, 1975, pp 58-66.

15. Suvorov, P. M.; Babushkin, V. I.; and Arkhangel'skiy, D. Yu. Ibid, No 3, 1976, pp 64-67.

16. Tikhomirov, Ye. P. Ibid, No 3, 1969, pp 71-75.

17. Suvorov, P. M. "Physiological Tests on Centrifuges in Medical Certification of Fitness for Flying and the Screening System," author abstract of doctoral dissertation, Moscow, 1969.

UDC: 612.843.312-06:612.745.1].014.47:531.15

HUMAN COLOR DISCRIMINATING FUNCTION WITH MUSCULAR TENSION DURING EXPOSURE TO VESTIBULAR STIMULI

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 41-44

[Article by Zh. M. Kudryashova and A. A. Shipov, submitted 10 May 79]

[English abstract from source]

Human studies have demonstrated that arbitrary tension of muscles (back and legs) during repeated vestibular exposures not only delays the development of motion sickness but also contributes to the maintenance of color discriminative stability of the visual function.

[Text] The safety of movement over all transport routes, including space flight routes, depends largely on the state of the operator's color vision. Yet the color discriminating function of the eyes of an individual performing operator work under specific conditions of exposure to unusual vestibular stimuli inherent in moving systems has not been studied at all.

In this work we tested color-discriminating function of the human eyes under conditions that are often encountered when operating ground and air types of transport, namely during tension of muscles of the shoulder girdle and legs during exposure to recurrent vestibular stimuli.

Methods

We conducted these studies on 50 individuals of both sexes ranging in age from 20 to 35 years.

Vestibular stimuli were simulated by the system of I. I. Bryanov [1]. The body was inclined and straightened during rotations with maximum concurrent tension of muscle groups of the shoulder girdle and legs. In all, there were 15 rounds of rotation. The test was stopped if grade II vestibulovegetative reactions (VVR-II--pallor, nausea, retching, hyperhidrosis) appeared during rotation.

As an objective record of autonomic reactions before and immediately after the vestibular test, we determined the heart rate (HR) according to the R-R interval on the EKG, maximum and minimum arterial pressure (APmin and APmax) according to N. S. Korotkov, caliber of central retinal veins and arteries (CCRV and CCRA) using a PEO-56 scope ["visuscope"], and pressure in the central retinal artery (PCRA) using an ophthalmodynamometer of the Krasnogvardeyets plant.

Color vision was evaluated on the basis of level of functional stability of color discrimination, spectral and color contrast sensitivity [2]. Color contrast sensitivity was tested in the long- (red, 665 nm), medium- (green, 530 nm) and short-wave (blue, 465 nm) bands of the visible spectrum. Spectral sensitivity was tested in the ranges of 665-655, 530-520 and 475-465 nm by determining the number of thresholds. Functional stability of color discrimination was studied by determination of time thresholds of adisparopia (ADP) with presentation of red-gray and blue-gray equations. Illumination of the test tables constituted 70-80 lx on white.

ADP was examined before rotations, in the intervals between them up through the 8th round, after the 10th and 15th rounds, as well as in the 5th, 10th and 15th min of the aftereffect period. Spectral and color contrast sensitivity was determined before, immediately after and 15 min after rotation. Background tests were made after adaptation for 10 min to white light, with mean spherical illumination in the room of 35-40 lx. The tests were made during the same time of year and day.

Muscular tension was not produced in the control studies.

Studies were also conducted with tension of muscles with the trunk tilted and straight, but without rotations.

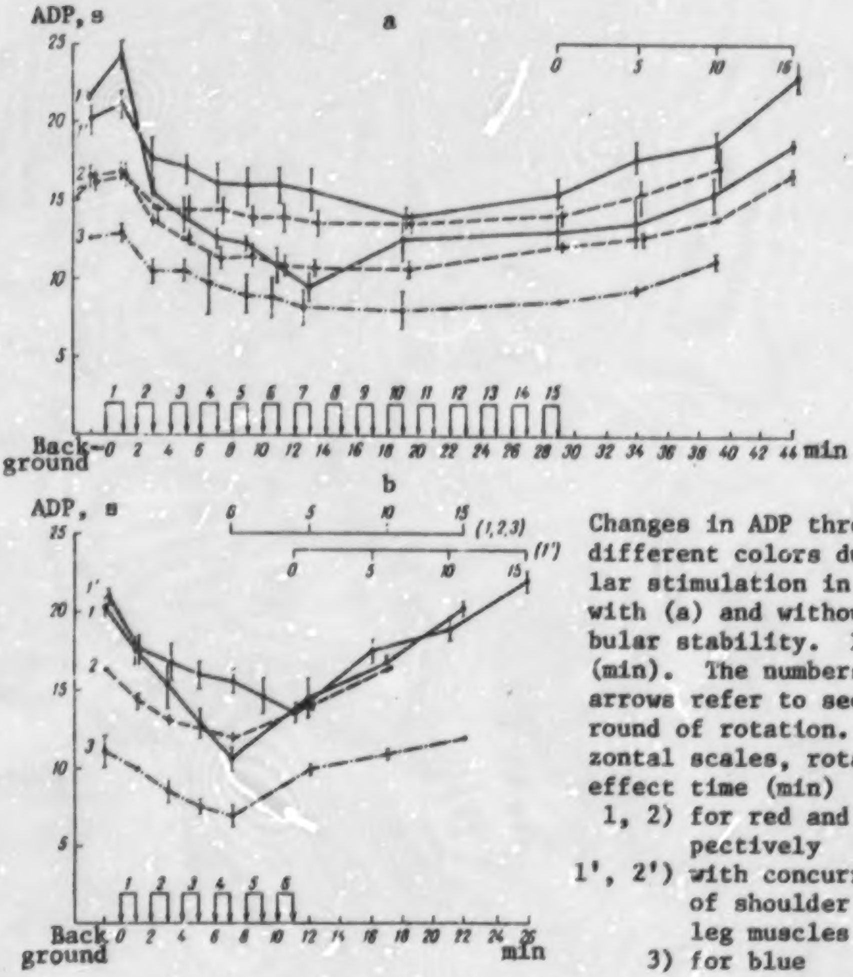
On the basis of analysis of the findings on subjects who failed to present clinically demonstrable vegetative reactions after 15 rounds of rotation, they were referred to the group with vestibular stability. Individuals who developed VVR-II in the course of control rotations made up the group with vestibular instability.

Our studies also made it possible to assess the effect of voluntary muscular tension on human vestibulovegetative stability.

The experimental data obtained were submitted to statistical processing, using the criterion of Student ($P<0.05$).

Results and Discussion

The change in ADP thresholds for different colors in both groups of subjects in the control series of studies (without muscular tension) is illustrated in the Figure and was described in detail by us previously [2].



Changes in ADP thresholds for different colors during vestibular stimulation in subjects with (a) and without (b) vestibular stability. X-axis, time (min). The numbers over the arrows refer to sequential round of rotation. Top horizontal scales, rotation aftereffect time (min)

1, 2) for red and blue, respectively
1', 2') with concurrent tension of shoulder girdle and leg muscles
3) for blue

The rate of decline of thresholds of color discrimination during muscular tension was substantially slower in the red and green bands of the spectrum in "vestibulostable" subjects (12 people), as compared to the control tests, while only a mild tendency toward slowing was noted in the blue band (see Figure, a). In the group with vestibular instability (38 people) there was also a decline in rate of decrease in thresholds for red (see Figure, b). In the blue-green part of the spectrum, no reliable differences from the findings in control tests were demonstrated.

Without rotations, bends with muscular tension (and without it) failed to elicit changes in color discrimination.

As can be seen in the Table, in stable individuals muscular tension did not alter the recorded autonomic reactions, as compared to those found in the control series of tests. At the same time, in individuals with vestibular instability, muscular tension neutralized the effects of vestibular stimulation according to virtually all parameters of peripheral and retinal circulation. They developed VVR-II only after the 6th round of rotation, rather than the 4th, as was recorded in the control series of tests (see Figure, b).

Parameters of peripheral and retinal circulation after exposure to vestibular stimuli

Test conditions	Group	PCRA, mm Hg	CCRV, µm	CCRA, µm	HR/min	APmin, mm Hg	APmax, mm Hg
Background	Vestibular stability	39±0,61	150±1,9	85±2,1	73,8±3,1	77,0±2,9	113,0±4,1
	Vestibular instability	39±0,87	146±2,1	83±1,8	74,5±2,5	78,0±2,1	115,0±1,84
Without muscle tension	Vestibular stability	44±2,4	150±1,8	80±1,9	71,5±2,5	75±2,1	110,4±3,8
	Vestibular instability	45±0,62	156±3,1	79±0,81	71,4±2,1	79,6±2,1	125±2,1
With muscle tension	Vestibular stability	40±0,7	150±1,8	82±2,3	78±1,5	80±1,7	110±2,3
	Vestibular instability	41±1,4	150±2,9	80±1,5	73±3,2	85,0±3,1	118,0±4,1

Thresholds of color and brightness contrast sensitivity did not change in either group, as in the control series of tests.

It is known that there is attenuation of many physiological reactions with static muscular tension. For example, there is depression of such a strong unconditioned reflex as retching after administration of apomorphine [3]. Static musuclar tension of the elevated arms with a weight eliminates the autonomic effect of vestibular stimuli, manifested by constriction of cutaneous vessels [4]. Voluntary tension of back muscles, as well as those of the legs, during exposure to vestibular stimuli analogous to those we used attenuated the autonomic symptoms of motion sickness [5].

The beneficial effect we demonstrated on voluntary muscular tension on vegetovestibular stability and chromatic vision with exposure to vestibular stimuli is apparently mediated by the cerebral cortex. Indeed, as has been comprehensively substantiated in [2], the decline of ADP thresholds for all colors, observed with repeated exposure to vestibular stimuli with relaxed muscles, is indicative of developing visual and general fatigue, and it is an indication of inhibitory processes in the visual cortex. The function of photoreceptors remains unaffected, since spectral and contrast color sensitivity, which characterize primarily the condition of the retina, remains virtually unchanged in both groups of subjects. A circumscribed focus of escitation appears in the motor cortex with voluntary tension of muscles, and it is sustained by formation of volitional impulses, on the one hand, and afferentation from proprioceptors and chemoreceptors of functioning muscles, on the other [6]. Brief muscular tension apparently creates favorable conditions for irradiation of excitation over the cortex, which delays development of inhibitory processes with repeated vestibular stimulation. In our opinion, for expressly this reason there is slower decline in level of stability of color vision. The inhibitory [7] function of the cortex, with reference to vegetovestibular reflexes, also remains more intact, for which reason there is delayed development of motion sickness.

Thus, voluntary tension of muscles (of the back and legs) during exposure to vestibular stimuli not only delays development of motion sickness, but attenuates the decline in level of color discriminating stability of vision.

BIBLIOGRAPHY

1. Bryanov, I. I. VOYEN.-MED. ZH. [Military Medical Journal], No 11, 1963, pp 54-56.

2. Kudryashova, Zh. M., and Shipov, A. A. KOSMICHESKAYA BIOL. [Space Biology], No 2, 1979, pp 25-31.

3. Sukhanov, A. A. BYULL. EKSPER. BIOL. [Bulletin of Experimental Biology], No 1, 1958, pp 14-18.

4. Rachkov, V. A. in "Motorno-vistseral'nyye is vistsero-motornyye refleksy" [Motovisceral and Visceromotor Reflexes], edited by M. R. Mogendovich, Perm', 1963, pp 203-213.

5. Ayzikov, G. S.; Yemel'yanov, M. D.; and Ovechkin, V. G. KOSMICHESKAYA BIOL., No 3, 1975, pp 68-74.

6. Vereshchagin, N. K. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 7, 1957, pp 699-704.

7. Khilov, K. L. "Function of Equilibrium Organ, and Motion Sickness," Leningrad, 1969.

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EFFECT OF TRANSVERSE ACCELERATIONS ON INNERVATION OF THE GUINEA PIG'S CRURAL SKELETAL MUSCLES

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No 3, 1980 pp 44-48

[Article by V. Ya. Osaulenko, submitted 20 Dec 78]

[English abstract from source]

Guinea-pigs were exposed to chest-to-back acceleration of 8 G for an hour. This exposure brought about significant morphological changes of a primary-reactive pattern in nerve elements of skeletal leg muscles. With time they enhanced: 6 hours and then 3 days after the experiment a small portion (1—1.5 %) of nerve fibers underwent fragmentation and degradation. Motor nerve endings showed the highest resistance. The first signs of restitution of changes in the peripheral nervous system were seen 6 days after the exposure. Nerve fibers did not return to the normal 9 days after the beginning of the experiment.

[Text] Many facts have been accumulated to date indicative of changes in the peripheral nervous system (PNS), blood vessels [1-7], atria [8-11], digestive tube [12-15], larynx [16], adrenals [17] and other internal organs under the influence of accelerations in different directions. However, there have been no studies of the effect of this same extreme factor on neural elements of skeletal muscles. In view of the foregoing, as well as the special role of the nervous system in maintaining structural integrity of muscles, our objective here was to study the state of the muscular nervous system after exposure to accelerations in the chest--back direction.

Methods

The material we studied consisted of leg muscles of 25 guinea pigs that had been exposed once to accelerations of 8 units (rotation on a centrifuge for 1 h) in the chest-back direction. During the experiment, 20% of the animals died. We collected material from them immediately after death was established. Other animals were sacrificed and material was collected from them immediately after rotation, then 6 h, 1, 3, 6 and 9 days later. Leg muscles of five intact animals served as a control. The material to be examined was fixed by submersion in 12% neutral formalin. Motor nerve fibers and their endings were demonstrated by various methods of silver nitrate impregnation (Bielschowsky-Gross, Schultze, Campos and others) followed by gold stain and additional staining of sections with hemalum and eosin. The myelin sheaths of myelinated fibers were demonstrated with hematoxylin varnish according to Spielmeyer.

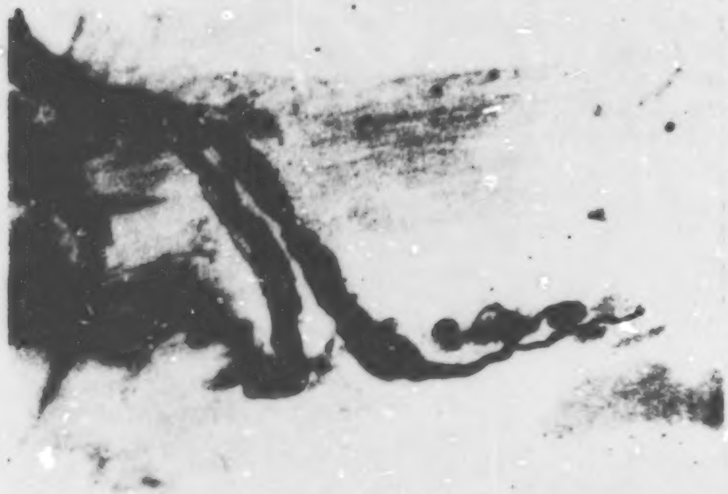

Figure 1. Reactive changes in nerve fibers (hyperimpregnation, swelling of axis cylinders and vacuolization of neuroplasm. Guina pig leg muscle after exposure to acceleration of 8 units for 1 h. Here and in Figures 2 and 3, Bielschowsky-Gross stain; microphotograph, MBI-6, ocular 7×, objective 40×

Results and Discussion

Examination of histological preparations of experimental material shows that single exposure to transverse accelerations with intensity of 8 units for 1 h elicits significant structural changes in the nerve elements of the animals' skeletal muscles. Overt signs thereof were demonstrable immediately after terminating the experiment, at which time they were of a primary, reactive nature. The most typical manifestations of PNS changes in these animals was distortion of impregnation properties (hyperimpregnation, dyschromia) of 95-97% of the nerve fibers of large, medium and even small caliber, as well as appearance of generalized or localized swellings along the course of nerve fibers of the first two sizes, appearance of bulges on their surface in the shape of mushrooms and spines, unravelling of neurofibril bundles at the sites of axonal thickening, and formation of centrally localized vacuoles as a result of hydropic neuroplasmic disturbances (Figure 1). As a rule, such fibers also present signs of irritation of Schwann's syncytium and unusual argyrophilia. The preterminal part of the motor nerve fibers was found to be the most labile, and it presented the most severe changes. As compared to others, the axis cylinders of small-caliber nerve fibers were very resistant. The motor nerve endings were particularly resistant to accelerations. During this stage of the observation period they retained entirely their inherent structure.

Six hours after exposure, PNS of the extremital skeletal muscles presented considerable deterioration. At this time, virtually all of its nerve fibers were altered. Moreover, in this group of guinea pigs, unlike the animals referable to the preceding examination time, some nerve fibers (about 1%) were subject to destruction and presented a state of fragmentation and granular breakdown. Concurrently, there was an increase in number of axons with signs of irritation, increase by one-third in number and size of congested elements in neuroplasm of the preterminal part of the nerve fibers. The motor endings of these animals, unlike those previously described, no longer consisted of a homogeneous group. Along with the usual motor plates, at this time we already encountered isolated motor nerve elements (no more than 2%) the terminal branchings of which were very strongly impregnated with silver and appeared thicker and coarser.

There was even more marked primary reactive changes in PNS of the crural skeletal muscles 1 day after exposure. However, we failed to detect new forms of changes, but there were qualitative and quantitative ones. It should be noted that, as compared to the preceding stage, nerve fibers with signs of dyschromia were encountered more often. Neuroplasmic congestion in the preterminal parts of many axons increased by 1.5-2 times in size. Although the number of vacuoles in nerve fibers did not change, they occupied chiefly a peripheral position, which is indicative of separation of these drops of fluid and subsequent elimination from fibers. We did not observe signs of destruction of new nerve fibers in this group of animals. As for the number of motor plates that were coarse, it increased by 2 times at this time, as compared to the preceding stage, constituting about 4% of those demonstrated. The result of the motor nerve endings retained their usual structure, which is indicative of considerable resistance of most of them to the factor in question.

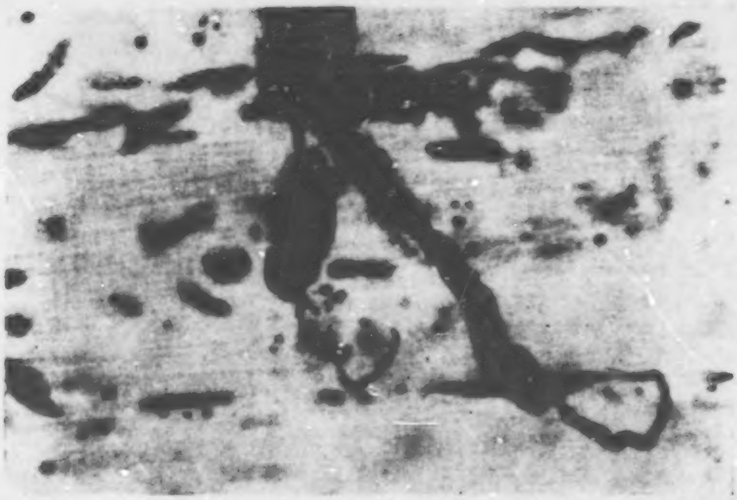

Figure 2. Formation of large accumulation of neuroplasm in preterminal part of nerve fiber; crural muscle of guinea pig 3 days after accelerations of 8 units for 1 h

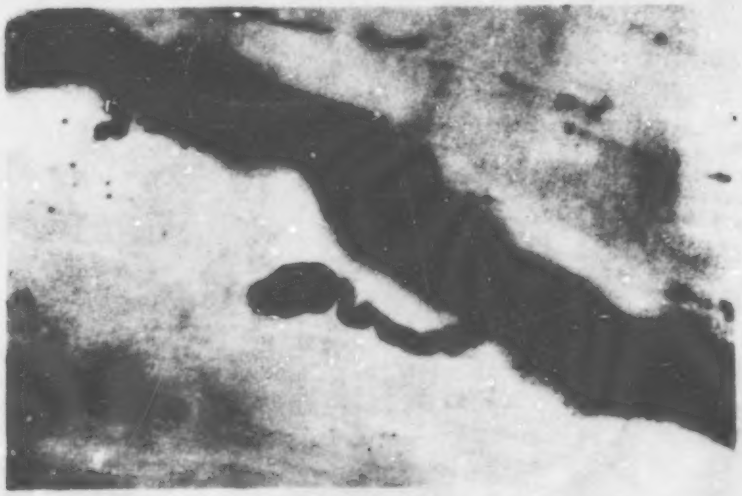

Figure 3. Neuroma in region of neuroplasmic congestion formed as a result of destruction of axonal terminal; guinea pig crural muscle 6 days after 8-unit accelerations for 1 h

Three days from the start of the experiment, there was further development of the previously described changes in the PNS of crural skeletal muscles. By this time there was enlargement of swellings of axis cylinders, mainly of thick myelinated nerve fibers. The vacuoles were encountered less often and usually situated in the superficial parts of the fiber. The neuroplasmic congestions of the preterminal part of the axons became larger, up to 40-50 μm in diameter (Figure 2). In this group of animals, we more often encountered nerve fibers in a state of degradation. The number of motor endings with signs of coarsening did not exceed 5% of the total number, even though it increased. The nerve endings of such plates appeared not only thicker than usual, but without the inherent loops, knobs or grids on the endings. The remaining 95% of the motor endings of skeletal muscles of this group of animals failed to reveal any visible changes.

Six days after exposure to accelerations, the changes in PNS of crural skeletal muscles consisted of essentially the same forms as before, but a significant part thereof showed regression. For this reason, the overall amount of changes occurring in the preceding periods diminished on the whole, and in some cases the nature thereof changed. Thus, the number of bulges on the surface of axis cylinders diminished to almost one-half, while the remaining spines and buds decreased in height; as a result the outlines of many nerve fibers were much smoother. There was a decrease in size of swellings of axis cylinders, and it is only in the preterminal part of some axons that there was occasional retention of large congestions of neuroplasma. As a result of separation of terminal elements from such fibers, they acquired the appearance of unique "neuromas," consisting of axons ending with considerable increase in diameter, to 50 μm (Figure 3). By this time, processes of elimination of products of disintegration of nerve fibers were concluded. No degradation of other nerves was observed at this time. The number of motor endings presenting signs of coarsening of terminals increased by 1-2%, as compared to the preceding stage, constituting 6-7% of those demonstrated.

After 9 days, processes of normalization of various elements of PNS of skeletal muscles were even more distinctly manifested. However, at this stage of our studies, some of the nerve fibers and their endings retained various signs of irritation (hyperimpregnation, dyschromia, small swellings, irregular outline of axis cylinders, coarse terminals in 6-7% of the motor plates, etc.).

Thus, the following conclusions can be derived on the basis of our observations: 1) single exposure to transverse (chest-back) accelerations of 8 units for 1 h continuously induces significant structural changes in the nerve elements of crural skeletal muscles, which do not disappear entirely, even after 9 days; 2) overt signs of changes in PNS of the crural skeletal muscles are demonstrable immediately after exposure to accelerations. Thereafter (after 7 h, 1, 3 and 6 days) they progress and extend over almost all nerve fibers of large, medium and, in part, small caliber; 3) PNS elements of skeletal muscles of the leg are subject mainly to primary reactive changes under the influence of single exposure to transverse accelerations, and they are only partially destroyed; 4) the preterminal segment is the most labile part of motor fibers exposed to accelerations; 5) the axis cylinders of small-caliber nerve fibers demonstrate high resistance to accelerations; 6) motor endings, which essentially retain their inherent structure, are particularly resistant to such conditions; 7) processes of restitution of altered nerve elements are slow, and they become noticeable 1 week after exposure to accelerations.

BIBLIOGRAPHY

1. Kurkovskiy, V. P. in "Voyen.-med.akad. im. S. M. Kirova. Sbornik referatov nauch. rabot za 1953-1955 gody" [Military Medical Academy imeni S. M. Kirov: Collection of Abstracts of Scientific Papers for 1953-1955], Leningrad, 1957, pp 106-108.

2. Nikolayeva-Luneva, L. N. "Sbornik trudov Tyumen. med. in-ta" [Collection of Works of Tyumen' Medical Institute], Vol 1, 1968, pp 137-141.

3. Klebanov, V. M. "Trudy Tselinograd. med. in-ta" [Works of Tselinograd Medical Institute], Vol 3, 1969, pp 83-84.

4. Rakhal'skiy, L. B. Ibid, pp 93-94.

5. Bardina, R. A.; Dyskin, Ye. A.; and Tikhonova, L. P. in "Mezhdunarordnyy kongress anatomov. 9-y. Tezisy dokladov" [Summaries of Papers Delivered at the 9th International Congress of Anatomists], Moscow, 1970, p 227.

6. Bardina, R. A.; Bayko, G. F.; Lev, I. D.; et al. in "Vsesoyuznyy s"yezd anatomov, gistologov i embriologov. 8-y. Tezisy" [Summaries of Papers Delivered at 8th All-Union Congress of Anatomists, Histologists and Embryologists], Tashkent, 1974, p 39.

7. Bayko, G. F.; Lev, I. D.; and Shadrina, N. S. in "Ukrainskaya resp. konf. anatomov, gistologov i embriologov. 7-ya. Tezisy dokladov" [Summaries of Papers Delivered at the 7th Ukrainian Republic Conference of Anatomists, Histologists and Embryologists], Khar'kov, 1976, p 11.

8. Yevloyev, S. I. in "Tselinograd. med. in-t. Nauch. konf. 1-ya. Materialy" [Proceedings of First Scientific Conference of the Tselinograd Medical Institute], Tselinograd, 1967, pp 65-66.

9. Yevloyev, S. I.; Klebanov, V. M.; and Mikhaylov, S. S. in "Mezhdunarodnyy kongress anatomov. 9-y. Tezisy dokladov," Moscow, 1970, p 229.

10. Prives, M. G.; Astakhova, V. V.; and Stepantsov, V. I. ARKH. ANAT. [Archives of Anatomy], No 5, 1970, pp 32-37.

11. Mikhaylov, S. S.; Klebanov, V. M.; and Yevloyev, S. I. Ibid, No 11, 1971, pp 37-47.

12. Oganesyan, T. G. in "Vliyaniye nekotorykh fizicheskikh i biologicheskikh faktorov na organizm" [Effects of Some Physical and Biological Factors on the Body], Moscow, 1965, pp 74-80.

13. Golev, V. P., and Chepelenko, G. V. ARKH. ANAT., No 11, 1971, pp 47-49. pp 47-49.

14. Tikhonova, L. L.; Konkin, I. F.; and Zlatitskaya, N. N. in "Vsesoyuznyy s"yezd anatomov, gistologov i embriologov. 8-y. Tezisy," Tashkent, 1974, p 373.

15. Konkin, I. F. ARKH. ANAT., No 7, 1975, pp 33-35.

16. Sudzilovskaya, Ye. F. Ibid, No 1, 1972, pp 95-96.

17. Klebanov, V. M., and Brindzyuk, V. P. "Trudy Tselinograd. med. in-ta," Vol 3, 1969, pp 91-92.

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STUDIES OF PROGNOSTIC SIGNIFICANCE OF ANTIORTHOSTATIC POSITION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 3, 1980 pp 48-54

[Article by Kh. Kh. Yarullin, V. A. Gornago, T. D. Vasil'yeva and
M. Ye. Gugushvili, submitted 19 May 78]

[English abstract from source]

The prognostic significance of head-down tilt at —15° and —30° for 6 min at each step was assessed in 40 normal men, aged 22—39. The study of mean values of the maximal amplitude, relative duration of the anacrotic phase, dicrotic and diastolic indices of hemispheric and bimastoidal rheoencephalography as well as of health condition helped to determine cerebral circulation in test subjects with good and moderate tolerance to head-down tilt and to define the criteria of tilt tolerance. The test subjects who showed good tolerance to head-down tilt displayed a simultaneous compensatory increase of the tone of large caliber arteries and arterioles that was accompanied by a noticeable increase in cerebral pulse blood filling at —15° and a moderate increase at —30° as well as the feeling of a slight blood rush to the head. The test subjects who displayed moderate tolerance to head-down tilt showed only an increase in the tone of large caliber vessels; they also exhibited a marked decrease in the tone of arterioles, venules and veins (especially at —30°) which was combined with a significant increase in the cerebral pulse blood filling and an appearance of marked venous waves on rheoencephalograms.

[Text] Rheographic studies of regional hemodynamics with an antiorthostatic [head-down tilt] test on crew members of Soyuz-12, Soyuz-13 and the Salyut-4 orbital station revealed that this test can be used to predict resistance of the circulatory system to weightlessness and, in the postflight period, to determine the degree of adjustment of the cardiovascular system to space flight conditions [1-6]. In addition, there is particularly distinct demonstration of the effect of hydrostatic pressure of the column of blood on central autonomic nerve elements in antiorthostatic position, which could also be used to assess self-regulation of cerebral circulation. Yet little study has been made of a number of questions dealing primarily with criteria for assessing endurance of the antiorthostatic test.

Methods

The antiorthostatic load constituted one-half the passive postural test on a turntable, and it consisted of two successive tilts to 15 and 30° from the horizontal plane, with the head down for 6 min in each position. Rheograms were recorded on a 4-channel 4RG-1M rheograph. The operating frequency of the rheograph was 120 kHz, current of 2.5 mA and voltage of 3 V. The method, which is based on an alternating current demodulating bridge, is accurate to 10%. We recorded concurrently the rheoencephalogram (REG) in the fronto- and bimastoidal leads, rheograms (RG) of the right lung and leg, as well as the EKG in the second standard lead; we measured arterial pressure (according to Korotkov). The method for analysis of RG was described previously [7].

Results and Discussion

We studied the prognostic value of antiorthostatic position on 40 healthy males ranging in age from 22 to 39 years.

Comparative analysis of clinical condition and severity of REG changes in the first few minutes of head down position (due mainly to hydrostatic effects), as well as compensatory hemodynamic changes (which developed in the 3d-5th min of the test) enabled us to make a distinction between two groups of subjects: one with good (1st group) and the other with satisfactory (2d group) endurance of the test. Each group consisted of 20 men.

The mean values of background regional RG indices of the 2d group were indicative of normal tonus and pulsed filling of vessels of the brain, lungs and leg. There was some increase in arteriolar and veinous tonus in the basin of the internal carotid artery and vertebrobasilar system, which was evident from the fact that the top range of the age-related norm was somewhat exceed by the dicrotic (DCI) and diastolic (DSI) indexes on hemisphere and bimastoidal REG (Figures 1 and 2).

The heart rate was slower (by a mean of 3/min) in head-down position. There was virtually no change in systolic arterial pressure, whereas diastolic pressure rose by a mean of 14.2 mm Hg ($P<0.05$), without clear-cut differences between the two groups. Consequently, pulse pressure dropped somewhat.

In the first group of subjects, the increase in mean maximum REG amplitude for the right hemisphere did not exceed 38.9% ($P<0.02$) with -15° tilt and constituted 94.4% ($P<0.01$) with -30° tilt, as compared to the background (see Figure 1), whereas it reached 66.3 and 124.9% ($P<0.001$), respectively in the second group.

Mean relative duration of the anacrotic phase ($\alpha/T\%$) of the hemisphere REG increased more in the first group, reaching 59.8% with -15° ($P<0.02$)

and 162.1% with -30° ($P<0.001$). In the second group, α/T% increased by 49.4 and 62.0% ($P<0.01$), respectively (see Figure 1).

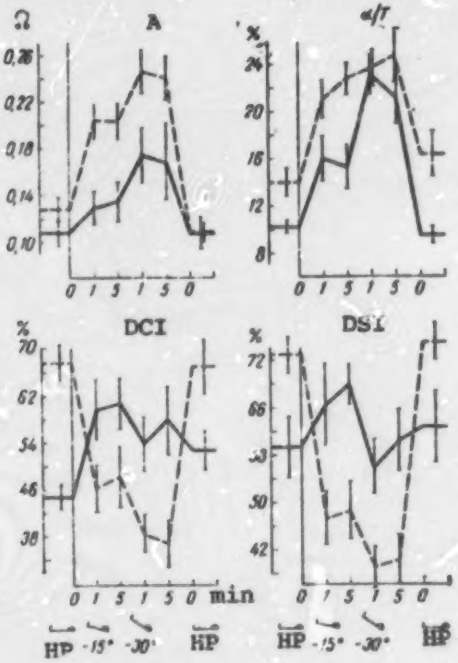

Figure 1.
Dynamics of mean values of maximum amplitude (A), α/T%, DCI and DSI on REG in right frontomastoid lead during stepped increases in head-down tilt, in the first (solid lines) and second (dash lines) groups

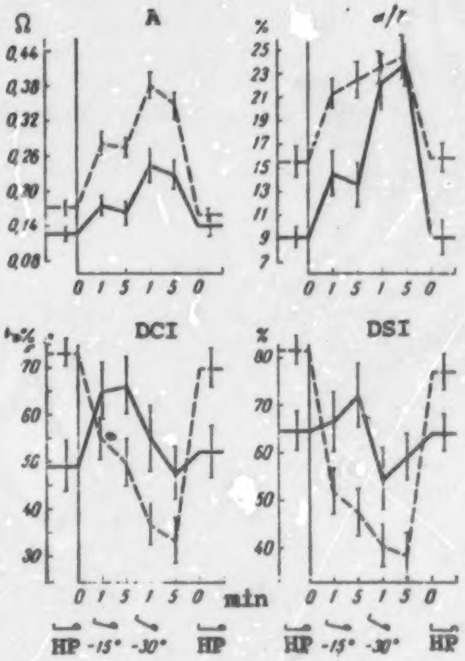

Figure 2.
Dynamics of mean values of maximum amplitude (A), α/T%, DCI and DSI on REG in bimastoidal lead during stepped increases in head-down tilt, in the first (solid lines) and second (dash lines) groups

In both figures: HP) horizontal position

There were more marked differences in changes of the REG dicrotic index between the first and second groups (see Figures 1 and 2). In the first group, there was an increase in mean DCI for the REG of the hemisphere to 35% ($P<0.05$) with a -15° angle and 12.1% with -30°, whereas in the second group the DCI dropped to 34.4 and 55.8%, respectively ($P<0.001$). Mean DSI of the hemisphere REG increased in the first group only with -15° tilt (to 11.4%), and decreased with -30°, but by no more than 15.1% ($P<0.5$) of the base value (see Figure 1); this parameter dropped by 41.6 and 52.8% ($P<0.01$), respectively, in the second group.

The increase in mean maximum amplitude of bimastoid REG in the first group did not exceed 24.1% ($P<0.5$) with -15° tilt and 61% ($P<0.02$) with -30° (see Figure 2); in the second group it reached 59.4 and 91.4% ($P<0.001$), respectively. The value of α/T% rose in the first group to 56.6% with -15° and 125.9% ($P<0.001$) with -30°; in the second group, to 49.4 and 62.1% ($P<0.01$), respectively. In the first group, DCI on the bimastoid REG (as compared to hemispheric REG) increased more with the stronger factor, and reached 29.3% ($P<0.05$) with a tilt angle of -30°; its decline by 45.4% ($P<0.001$) in the second group was lesser than on hemispheric REG. As in the hemispheric REG, DSI rose only in the first group with a -15° tilt, reaching 14.3%; the decline was less marked than on the REG of the hemisphere, and did not exceed 35.1 and 46.5% ($P<0.001$), respectively.

During head-down position, there was some increase in pulsed filling of the right lung with blood, against the background of negligible decrease in tonus of large arteries and arterioles. In the second group, it decreased insignificantly, with concurrent slight increase in tonus of large vessels and decrease in arteriolar tonus. The changes in DSI, i.e., in tonus and pulsed filling of pulmonary veins, were minimal and also dissimilar.

There was an appreciable increase in pulsed delivery of blood to the leg in head-down position, to 35% of the base level in the first group and 28% in the second, against the background of elevation of arteriolar tonus (DCI, by 19.4 and 52%). However, these differences between groups, as those in the lung RG, were unreliable.

Thus, during stepped increase in angle of head-down tilt, we demonstrated reliable changes in indices of fronto- and bimastoid REG in both groups. We found a reliable difference between these groups of healthy subjects in mean DCI, DSI, maximum amplitude and α/T% on hemispheric and bimastoid REG with tilt angles not only of -30° but -15°. The dynamics of these REG parameters indicate that concurrent compensatory increase in tonus of arterioles and arteries of large caliber, associated with significant increase in pulsed filling with -15° tilt and moderate with -30°, were inherent in individuals of the first group. The negligible decline of DSI, i.e., venous tonus, only with -30° also confirmed the rather effective counteraction of cerebral vessels to overfilling with blood. This state of compensated intracranial stasis was associated with some sensation of blood rushing to the head, pulsation in the temples, flushed face and injected scleral vessels.

In the second group of subjects, there was only marked increase in tonus of vessels of large caliber; the indices of tonus of arterioles (DCI), venules and veins (DSI) dropped appreciably, particularly with a -30° tilt angle, and they were not infrequently associated with appearance of distinct venous waves on the REG. This state of moderate arteriolar and venous stasis was associated with the sensation of marked rush of blood to the head and even a feeling of cranial swelling ["bursting"], fever, pulsation of veins of the head, engorgement of cervical veins and hyperemia of the sclera, face and neck with a -30° tilt.

As we see, as compared to systemic and pulmonary hemodynamics, regional cerebral circulation reflects more specifically the compensatory and adaptational changes in regulation under the influence of antiorthostatic position. Dilatation of cerebral vessels leads to secondary increase in precapillary resistance and sphincter tonus, thereby counteracting dilatation and reduction in length of the open capillary bed [8], reducing to a minimum the signs of intracranial plethora. In other words, after the first minutes in head-down position with different tilt angles, the increasing venous stasis leads, by virtue of an arteriovenous reflex [9], to compensatory restriction of arterial influx to the brain [5, 10-12], due to increased tonus of vessels of large and medium caliber, as well as arterioles. This was indicated by the significant increase in α/T% and DCI.

As we know, maximum hydraulic resistance of the vascular system is referable to small arteries and arterioles [13-17]. In the brain, these vessels have a thick adventitia [muscular layer], and for this reason they play the role of the main element in regulation of cerebral circulation [17, 18]. Reduction of the lumen of precapillary arterioles has a more significant effect onvolumetric rate of cerebral blood flow than analogous changes in radius of other vessels [17]. This is the reason for the great informativeness of REG DCI, which reflects mainly the tonus of arterioles [7, 17, 19-23] as a criterion of endurance of head-down position associated with changes in perfusion and transmural pressure. Systemic and particularly regional arterial pressure is maintained chiefly by the arterioles with the use of postural factors [2, 5, 24, 25].

In the opinion of G. I. Mchedlishvili [11], the constrictive reaction of great vessels and, in part, pial arteries is the compensatory mechanism that prevents development of venous stasis in the brain, in addition to the system of collateral circulation. This was manifested on the REG of subjects in both groups by a drastic increase in α/T%, the indicator of tonus of large and medium caliber arteries [7, 19, 20], which is directed toward attenuating the excessive cerebral hyperemia. This is why α/T% was also an informative criterion of endurance of antiorthostatic position.

The effectiveness of the above mechanisms, which counteracted plethora of cerebral vessels, was distinctly manifested in the first group of subjects, whereas in the second group there was merely a significant increase in tonus of large and medium caliber vessels, with concurrent appreciable decrease in tonus of cerebral arterioles, venules and veins. The gradual decline of transmural pressure in cerebral vessels elicited moderate autoregulatory dilation thereof in order to maintain cerebral blood flow [26].

However, with such cerebral vasodilatation, even a minor elevation of systemic arterial pressure could cause further elevation of intracranial pressure, and it could be a factor that damages brain tissue [27]. Consequently, the demonstrated hypotonia of cerebral arterioles and veins, associated with subcompensated venous stasis in the brain, is indicative of some weakening of mechanisms of self-regulation of cerebral circulation in antiorthostatic position [2, 5, 28, 29], i.e., diminished functional capabilities of the cardiovascular system of subjects in the second group, as compared to the first. This confirms the prognostic value not only of DCI, but DSI on the REG, the indices of venous tonus and efflux, in head-down position [7, 10, 17, 19, 20, 30]. Constriction of cerebral veins, along with constriction of arterioles, diminishes influx of blood and capacity of the cerebral venous system [12, 31], thus stabilizing cerebral circulation [16].

As we see, the dynamics of α/T%, DSI and particularly DCI, as well as of maximum REG amplitude, which provide objective data on differences in endurance of head-down position, could serve as a reliable prognostic criterion for evaluation of the state of antigravity compensatory mechanisms of the cerebrovascular system as related to different postural tests. The dynamics of maximum REG amplitude, which reflects the pulsed increment in delivery of blood to the brain, make it possible to determine the severity of plethora in head-down position. The dynamics of α/T%, DCI and DSI, which reflect tonus of large arteries, precapillary and postcapillary vessels (arterioles, venules and veins), respectively, permit determination of the nature of cerebral hemodynamic changes during such tests.

Analysis of the dynamics of mean values for this indices of hemispheric and bimastoid REG's, as well as the physical condition of the subjects, enabled us to describe cerebral circulation in the case of good and satisfactory endurance of head-down tilting at angles increasing in steps, and to define the criteria of endurance of this test.

The criteria of good endurance of stepped increases in angle of head-down position are as follows: good subjective tolerance of the test (sensation of slight rush of blood to the head, pulsation of the temples, flushed face and erythremic sclera); appreciable elevation of DCI, the indicator of tonus of small arteries and arterioles (by 35% of the base level); increase in α/T%, the indicator of tonus of vessels with large and medium caliber by over 100%; increased pulsed delivery of blood, by 100% to the hemisphere and by 60% to the vertebrobasilar system; elevation or absence of change in DSI, index of tonus of venules and veins.

The criteria of satisfactory endurance of the test are: some discomfort (sensation of rush of blood and "bursting" in the head, fever, pulsation of veins, swelling of cervical veins, hyperemia of the face, sclera and neck); visible decrease in tonus of arterioles and small arteries (DCI, by 28-55%); visible decrease in venous tonus (DSI, by 35-52%); increase to 80% in α/T%; increased pulsed delivery of blood, by more than 100% to hemispheres and more than 80% to the vertebrobasilar system.

The above criteria indicate that this test can be used to assess the functional capabilities of the cardiovascular system and efficiency of its antigravity mechanisms, i.e., to predict antiorthostatic stability of the body. This prompted us to use the test in screening cosmonaut candidates, as well as in preflight and postflight examinations of cosmonauts. The findings of the latter confirmed the efficacy of this test both to predict resistance of the circulatory system, particularly cerebral hemodynamics, to weightlessness, and to determine the nature and degree of changes in regulation thereof under the influence of space flight factors [2-5]. Since antiorthostatic position restricts, as we have shown above, the range (top) of self-regulation of cerebral circulation, the REG dynamics during this test can aid in detection of latent functional deficiency, primarily of its regulatory mechanisms.

BIBLIOGRAPHY

1. Vorob'yev, Ye. I.; Gazenko, O. G.; Gurovskiy, N. N.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1976, pp 3-18.

2. Yarullin, Kh. Kh.; Vasil'yeva, T. D.; Krupina, T. N.; et al. Ibid, No 2, pp 22-30.

3. Kalinichenko, V. V.; Asyamalov, B. F.; and Zhernavkov, A. F. Ibid, No 5, pp 18-23.

4. Kakurin, L. I., et al. in "Kosmicheskiye polety na korablyakh 'Soyuz.' Biomeditsinskiye issledovaniya" [Space flights Aboard Soyuz Series Spacecraft. Biomedical Studies], Moscow, 1976, pp 230-265.

5. Yarullin, Kh. Kh., and Vasil'yeva, T. D. KOSMICHESKAYA BIOL., No 3, 1977, pp 20-26.

6. Alekseyev, D. A.; Yarullin, Kh. Kh.; Krupina, T. N.; et al. Ibid, No 5, 1974, pp 56-72.

7. Yarullin, Kh. Kh.; Krupina, T. N.; and Vasil'yeva, T. D. Ibid, No 4, 1972, pp 33-39.

8. Folkov, B., and Nilk E. "Circulation," Moscow, 1976.

9. Wamada, S., and Burton, A. C. J. APPL. PHYSIOL., Vol 6, 1954, pp 501-505.

10. Moskalenko, Yu. Ye.; Vaynshteyn, G. B.; and Kas'yan, I. I. "Intracranial Circulation in the Presence of Accelerations and Weightlessness," Moscow, 1971.

11. Mchedlishvili, G. I. "Cerebral Arteriospasm," Tbilisi, 1977.

12. Kholodenko, M. I. "Venous Circulatory Disorders in the Brain," Moscow, 1963.

13. Savitskiy, N. N. "Some Methods of Studying and Making a Functional Assessment of the Circulatory System," Leningrad, 1956.

14. Wiggers, K. "Dynamics of Circulation," Moscow, 1957.

15. Burton, A. C. "Physiology and Biophysics of the Circulation," Chicago, 1965.

16. Kislyakov, Yu. Ya. "Mathematical Modeling of Cerebral Circulation and Exchange of Gases," Leningrad, 1975.

17. Sokolova, I, V.; Yarullin, Kh. Kh.; Maksimenko, I. M.; et al. ZH. NEVROPATOL. I PSIKHIATR. [Journal of Neuropathology and Psychiatry], No 9, 1977, pp 1314-1321.

18. Fog, M. J. NEUROL. PSYCHIATR., Vol 1, 1938, pp 187-197.

19. Yarullin, Kh. Kh. in "Klinicheskaya neyrofiziologiya" [Clinical Neurophysiology], Leningrad, 1972, pp 544-559.

20. Eninya, G. I. "Rheography as a Technique for Evaluating Cerebral Circulation," Riga, 1973.

21. Donzelot, E.; Milovanovich, J. B.; and Meyer-Heine, A. ARCH. MAL. COEUR [Archives of Heart Disease], Vol 11, 1950, pp 1013-1016.

22. Chlebus, H. AM. HEART J., Vol 64, 1962, pp 22-32.

23. Mukhamedrakhimov, F. F. EKSPER. KHIR. [Experimental Surgery], No 3, 1966, pp 10-13.

2[illegible]. Samueloff, S. L.; Browse, N. L.; and Shapherd, J. T. J. APPL. PHYSIOLW, Vol 21, 1966, pp 47-54.

25. Kupriyanov, V. V.; Karaganov, Ya. L.; and Kozlov, V. I. "The Microcirculatory System," Moscow, 1975.

26. Kety, S. S. in "Handbook of Physiology, Sect. 1: Neurophysiology," Washington, Vol 3, 1960, pp 1751-1760.

27. Hamer, J., et al. J. NEUROSURG., Vol 46, 1977, pp 36-45.

28. Lassen, N. A. CIRCULAT. RES., Vol 15, Suppl 1, 1964, pp 201-204.

29. Meyer, J. S., et al. STROKE, Vol 4, 1972, pp 187-200.

30. Meyer-Heine, A.; Giblin, S.; and Dessertenne, G. ARCH. MAL. COEUR, Vol 42, 1949, pp 337-351.

31. Johnson, J. H., and Rowan, J. O. J. NEUROL. NEUROSURG. PSYCHIAT., Vol 37, 1974, pp 392-402.

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EVALUATION OF EFFICACY OF THE SET OF PREVENTIVE MEASURES REFERABLE TO THE HUMAN NEUROMUSCULAR SYSTEM UNDER HYPOKINETIC CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 3, 1980 pp 54-57

[Article by V. A. Tishler, V. I. Safonov and Z. A. Krivitsina, submitted 4 Jan 79]

[English abstract from source]

The study of excitability and lability of the musculus rectus femoris was used to evaluate efficiency of exercises during bed rest. A combination of exercises with other countermeasures did not reduce their prophylactic effect.

[Text] The results of medical studies conducted on the Salyut and Skylab programs revealed that the physiological changes occuring under the influence of flight factors can be adequately compensated and prevented with various preventive agents [1-7].

The fact that changes occur in the same direction after space flights and ground-based model experiments simulating some of the physiological effects of weightlessness makes it possible to evaluate various preventive measures on the model of hypokinesia [8, 9].

Many researchers believe that physical exercise is an effective means of preventing hypokinetic disorders [10-14].

Our objective here was to assess the efficacy of physical exercise (both by itself and in conjunction with other preventive steps) on the basis of excitability and lability of skeletal muscles in the course of 49 days of antiorthostatic (head-down) hypokinesia (ANOH).

Methods

Excitability and lability of the neuromuscular system (NMS) were tested by the method of electrostimulation, which was described in detail previously [15]. We determined the excitation threshold, i.e., the rheobase, as well as optimum and maximum rhythm of stimulation of the femoral rectus muscle, twice in the background period, then on the 5th, 19th, 33d and 47th days of ANOH (-4°). In the first series of tests (6 people), the subjects exercised on a combination athletic exercizing unit (CAE) to prevent hypokinetic disorders. In the second series (6 people), in addition to physical exercise (on the CAE), we used conditioning with creation of lower body negative pressure (LBNP), and the subjects were given fluid and salt supplements ($NaCl + H_2O$).

In the third series (6 people), hypokinetic disorders were corrected by means of a set of preventive measures (exercise on the CAE, with LBNP, intake of water and salt supplement). In addition, pharmacological agents were used: 20 mg ephedrine and 1 mg strychnine daily given to all 6 subjects from the 15th to 25th days, and to 3 of them from the 39th to 49th days. L. I. Kakurin et al. [9] described in detail the preventive steps taken in the first, second and third series of tests. The fourth series (36 people) was a control (no preventive steps taken).

Results and Discussion

The dynamics of the rheobase of the femoral rectus muscle, illustrated in Figure 1, for all four series indicate that there was the same direction of changes in all series where preventive steps were taken. The highest, but insignificant elevation of threshold of stimulation was observed in the middle of the period of hypokinesia, on the 19th day for subjects in the 1st-3d series and 33d day in the 1st and 2d series. At the end of the hypokinetic period, excitability of the femoral rectus increased, to approximately the base value in the 1st and 2d series, and even somewhat higher in the 3d series. Unlike this, the decline of excitability in subjects of the 4th series progressed substantially with increase in duration of hypokinesia.

A comparative analysis of the parameters characterizing the lability of the NMS in subjects who only exercised on the CAE, with the use of the set of preventive measures and without them is illustrated in Figures 2 and 3.

Figure 2 shows that the optimum rhythm of stimulation of the femoral rectus changed insignificantly during hypokinesia in subjects of the series where preventive measures were used. A maximum tendency toward decline of this parameter was observed on the 5th day of hypokinesia in subjects for whom a set of preventive measures was used without pharmacological agents (by 16%, as compared to the base value). On the 19th, 33d and 47th days of hypokinesia, the tendency toward decline was more marked in subjects who only exercised on the CAE (by 10, 11 and 4%, respectively). In individuals who were submitted to the set of preventive measures without pharmacological agents, the optimum rhythm of stimulation decreased by 3% on the 19th day of hypokinesia, as compared to the base level, whereas in the series where pharmacological agents were used it increased by 2%. Conversely, on the 33d day of hypokinesia, this parameter decreased by 8% with the use of pharmacological agents, and it increased by 4% in the series without such agents. On the 47th day of hypokinesia, the optimum rhythm of stimulation increased by a mean of 3% in both series where the complex of preventive measures was used. In contrast, the optimum rhythm of excitation in the 4th series of subjects began to decline on the 5th day of hypokinesia, constituting 50% of the base level on the 47th day thereof.

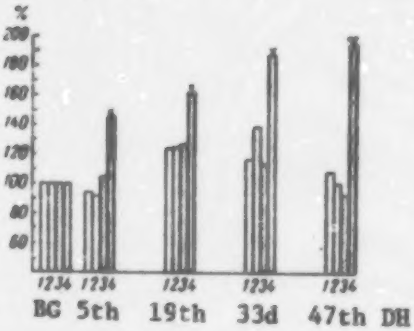

Figure 1.
Dynamics of relative change in rheobase of femoral rectus (base data—100%). Here and in Figures 2 and 3: 1-4) 1st, 2d, 3d and 4th series The "x" refers to reliable data ($P<0.05$). DH—day of hypokinesia; BG—background.

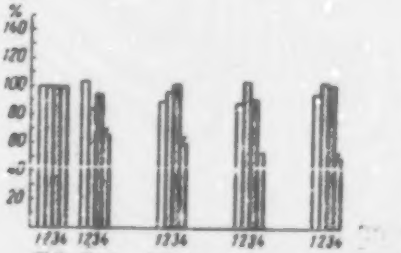

Figure 2.
Dynamics of relative change in optimum rhythm of femoral rectus (base data—100%)

Figure 3 illustrates the dynamics of maximum rhythm of excitation of the femoral rectus in subjects of all four series. There was the least decrease in maximum rhythm in subjects who only exercised on the CAE, and on the 5th, while on the 5th and 33d days of hypokinesia it even exceeded the base level (by 17 and 3%, respectively). The changes in maximum rhythm of excitation were about the same on the 19th and 33d days of hypokinesia in the subjects for whom a set of preventive measures was used. On the 5th and 47th days of hypokinesia, maximum rhythm declined more in the series with the set of preventive measures without pharmacological agents, and this decline was substantial on the 5th day of hypokinesia.

Thus, comparative analysis of changes in excitability and lability of the neuromuscular system of subjects referable to the four series demonstrated significant differences between the series where preventive steps were taken and where they were not. In the fourth series, excitability and lability diminished significantly starting on the 5th day of hypokinesia. In the series with use of preventive measures, the changes were insignificant, with the exception of the decrease in maximum rhythm of excitation on the 5th day of hypokinesia

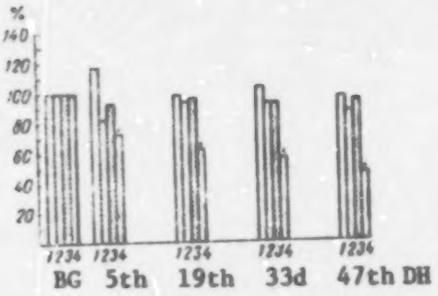

Figure 3.
Dynamics of relative changes in maximum rhythm of the femoral rectus (base data--100%)

in subjects of the first and second series, that could not be attributed to the preventive measures, since LBNP and the fluid and salt supplement were not used at the first stage of hypokinesia.

Comparative analysis of parameters characterizing excitability and lability of the NMA of subjects who only exercised on the CAE, as well as those who followed the sets of preventive measures, revealed that these parameters undergo essentially insignificant changes during hypokinesia.

Retention of excitability and lability of the NMA, which was found in this study, along with retention of force of flexor and extensor muscles (10 muscle groups were tested), leads us to the conclusion that physical exercise is the chief means of preventing hypokinetic disorders of the NMA. Combination thereof with other preventive measures modifies insignificantly, but does not attenuate the preventive effect of exercising the human NMA.

BIBLIOGRAPHY

1. Vasil'yev, P. V. in "Nevesomost'" [Weightlessness], Moscow, 1974, pp 278-296.

2. Genin, A. M., and Pestov, I. D. in "Chelovek v kosmose" [Man in Space], Moscow, 1971, p 6.

3. Idem, Ibid, 1974, pp 76-90.

4. Pestov, I. D., and Asyamolov, B. F. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1972, pp 59-64.

5. Bestov, I. D., and Geratevol', Z. Dzh. in "Osnovy kosmicheskoy biologii i meditsiny" [Fundamentals of Space Biology and Medicine], Moscow, Vol 2, Bk 1, 1975, pp 324-269.

6. McCally, N.; Piemme, T. E.; and Murray, R. H. AEROSPACE MED., Vol 37, 1966, pp 1247-1249.

7. McCally, M.; Pohl, S. A.; and Sampson, P. A. Ibid, Vol 39, 1968. pp 722-733.

8. Genin, A. M., and Kakurin, L. I. KOSMICHESKAYA BIOL., No 4, 1972, pp 26-28.

9. Kakurin, L. I.; Katkovskiy, B. S.; Tishler, V. A.; et al. Ibid, No 3, 1978, pp 20-27.

10. Brannon, E. W.; Kockwood, C. A.; and Potts, P. AEROSPACE MED., Vol 34, 1963, pp 900-906.

11. Yeremin, A. V.; Bazhanov, V. V.; Marishchuk, V. L.; et al. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 13, 1969, pp 191-199.

12. Stepantsov, V. I.; Tikhonov, M. A.; and Yeremin, A. V. KOSMICHESKAYA BIOL., No 4, 1972, pp 64-68.

13. Idem, in "Nevesomost'," Moscow, 1974, pp 298-313.

14. Tishler, V. A.; Anashkin, O. D.; Pervushin, V. I.; et al. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, Vol 2, 1975, pp 190-192.

15. Titov, G. A. in "Problemy sportivnoy meditsiny. Metody vrachebno-fiziologicheskikh issledovaniy sportsmenov" [Problems of Sports Medicine: Methods of Medical and Physiological Studies of Athletes], Moscow, 1972, pp 35-40.

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THE STRESS REACTION TO HYPOKINESIA AND ITS EFFECT ON GENERAL RESISTANCE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 57-60

[Article by I. P. Chernov, submitted 30 Sep 78]

[English abstract from source]

Rat experiments have demonstrated that the development of the hypokinetic syndrome involves occurrence of a three-stage stress reaction characterized by a change in the general health state, body mass, and activity of the hypothalamic-pituitary-adrenal system. The hypokinetic stress affects total resistance and ionizing radiation sensitivity of animals. At a certain stage of development the hypokinetic stress contributes to the state of elevated "cross" resistance.

[Text] The data in the literature indicate that hypokinesia, which combines isolation and restricted muscular activity, elicits a stress reaction in man and animals [1-3]. It appears in response to depression of the "freedom instinct."

In this work, we have tried to trace the chronology of dynamic manifestations of the stress reaction on different levels of biological integration, and to demonstrate their correlation and influence on the body's general resistance.

Methods

Experiments were conducted on 250 male mongrel rats with an initial weight of 150-170 g. To create hypokinetic conditions, the animals were placed in box cages made of plexiglas, which restricted movement in all directions. We decapitated 6 rats from the experimental group and the same number from the control group after 3 h, 1, 3, 5, 10, 20, 30, 45, 60, 75 and 90 days. We evaluated the severity of stress and general resistance on the basis of the animals' general condition, weight (checked daily), condition of the system of the hypothalamus-hypophysis-adrenals, and sensitivity to ionizing radiation. Proof of the informativeness of the indicators we selected has been offered in a number of works [4-6]. The rats were exposed to total-body radiation from a Luch unit (dosage 800 rad and dose rate 65 rad/min). The first group of animals was irradiated on the 3d day of hypokinesia, against the background of weight loss and significant elevation of 11-HCC [hydroxycorticosteroids] (to 13.83±0.002 $\mu g\%$, versus 6.3±0.002 μg in the control). The second and third groups were exposed to radiation on the 20th day of hypokinesia and 3d day of the recovery period after 20-day hypokinesia, respectively. Rats kept in the vivarium prior to irradiation served as a control. On the 45th day, we determined the percentage of deaths and survivals in each group of animals. In all series of this study, we recorded the weight of the hypophysis and right adrenal. Karyometry of neurons of the arcuate nucleus of the hypothalamus and cells of the fascicular zone of the adrenals was performed on sections stained with cresyl violet. At each time, we measured 100 nuclei from each of 4 animals. We used an MOV-1-15^x ocular micrometer to measure the large (L) and small (B) diameters. The volume was determined using the following formula:

$$V = \frac{\pi}{6} LB^2$$

Weight and karyometric data were submitted to statistical processing [7, 8], and the reliability of differences was determined according to the criterion of Student (with $P<0.05$).

Results and Discussion

The rats were submitted to hypokinesia during the first days of brief motor excitement; on the next days (5th-10th days) we observed a decrease in motor activity, attenuation of the food reflex, diarrhea and shedding of fur. The animals then gradually adjusted to the new conditions, became more active, neat and consumed their feed willingly. In the 3d month of the experiment, we observed depression of motor activity and worsening of the animals' general condition.

The rats kept under the usual vivarium conditions gained weight progressively (Fiugre 1), reflecting prevalence of assimilation processes. Under hypokinetic conditions, the dynamics of body weight presented fluctuations: At the early stages weight dropped (with a peak on the 3d day), then it reverted to the base level (10th day), with subsequent (on the 10th-45th days) stabilization at slightly above base levels. In the 3d month of hypokinesia, body weight began to drop again. At the end of the experiment, the difference between wieght of experimental and control rats constituted 170 g.

The observed undulant changes in body weight and general condition of the animals during hypokinesia are typical of the stress reaction that occurs under the prolonged effect of deleterious factors. In particular, such dynamics of rat weight were observed during prolonged, graduated electric stimulation [5]. The slower growth of animals with stress is attributed to impaired balance of metabolic processes in the direction of prevalence of dissimilation, dehydration of the body and mobilization of fat from the fat depots. All these changes inherent in stress have been repeatedly observed under hypokinetic conditions [9, 10].

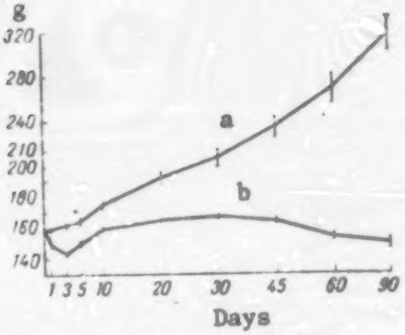

Figure 1.
Dynamics of weight change in control (a) and hypokinetic (b) rats; x-axis, day of examination; y-axis weight (g)

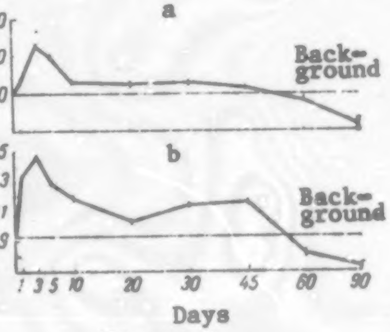

Figure 2.
Dynamics of relative weight of pituitary (a) and adrenals (b) under hypokinetic conditions; x-axis, day of examination; y-axis, weight (μg)/100 g body wt.

Analysis of relative weight of the hypophysis and adrenals revealed the same phasic nature as demonstrated for the animals' general condition and body weight (Figure 2), and this was clearly demonstrable on the tissular level. We must, however, indicate that the changes in weight of the pituitary and adrenals, as well as mean volume of neurons of the hypothalamic arcuate nucleus and cells of the fascicular zone of the adrenals, were in the opposite direction from those in body weight at the early stages of hypokinesia and in the same direction thereafter.

In view of the fact that the weight of endocrine organs is often correlated with function, while nucleus volume is a reliable criterion of secretory function of neurons [11] and the adrenal cortex [12], our conclusions pertaining to the phasic nature of changes in the hypothalamo-hypophyseo-adrenal system under hypokinetic conditions also extend to functional activity of this system. The nature and direction of changes in this system, as well as the fluctuations of body weight and general condition of the rats, indicate that a three-phase stress reaction develops in the course of formation of the hypokinetic syndrome, with periods of mobilization (first 10 days), resistance or "chronic resistance" (20-30 days) and a period of gradual depletion of the animals' potential for adjustment. The latter is manifested with particular distinction in the 3d month of the experiment. Such a chronology of hypokinetic stress was described by Ye. A. Kovalenko [3].

The fluctuations in general resistance under hypokinetic conditions were demonstrable when ionizing radiation was used as a test of rat sensitivity. Survival of rats exposed to radiation without additional factors (control group, 20 animals) constituted 30±10.1% by the 45th day, and death occurred at the height of radiation sickness (10th-20th days). The survival rate for animals exposed to radiation during the period of mobilization of hypokinetic stress (3d day, 26 animals) differed from the control without statistical reliability ($P>0.2$). However, the earlier death of animals in this group (mainly on the 5th-10th days) and slow weight gain by surviving rats (151±6.9 g on the 45th day, versus 200±5.0 g in the control) are indicative of some decrease in resistance to ionizing radiation during this period. The survival rate rose to 75±8.2% ($P<0.001$) and deaths occurred at a later time in the group of 28 rats exposed to radiation on the 20th day of hypokinesia. Such fluctuation of radiosensitivity of rats was demonstrated on the model of prolonged stress induced by graduated electrostimulation [5]. The authors showed that rat sensitivity to ionizing radiation increased at the stages of mobilization and depletion, and decreased at the resistance stage.

There are different mechanisms involved in formation of heightened "cross" resistance of the body associated with the stress reaction [13, 14]. It is important to note that it persisted for some time even after discontinuing exposure to the stimulus [15]. The latter thesis is consistent with our data, where increased resistance to radiation (exposure to radiation of 24 rats on the 3d day after 20-day hypokinesia; survival rate 58.3±10.1%) persisted during the period of readaptation.

Thus, in the course of formation of the hypokinetic syndrome, a three-phase stress reaction develops, which is manifested by the changes that are typical of this reaction: in general condition of the organism, body weight, activity of the hypothalamo-hypophyseo-adrenal system. Hypokinetic stress has a substantial effect on formation of general body resistance and its sensitivity to ionizing radiation. At a certain stage of its development, hypokinetic stress forms a state of heightened cross resistance.

BIBLIOGRAPHY

1. Portugalov, V. V.; Gazenko, O. G.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1967, pp 18-25.

2. Kosmolinskiy, F. P. "Emotional Stress During Work Under Extreme Conditions," Moscow, 1976.

3. Kovalenko, Ye. A. PAT. FIZIOL. [Pathological Physiology], No 3, 1975, pp 11-24.

4. Gorizontov, P. D. BME [Great Medical Encyclopedia], Moscow, Vol 1, 1976, pp 188-192.

5. Gorizontov, P. D., and Rudakov, I. A. PAT. FIZIOL., No 2, 1964, pp 17-22.

6. Aleshin, B. V. in "Gomeostaz" [Homeostasis], Moscow, 1976, pp 60-92.

7. Oyvin, I. A. PAT. FIZIOL., No 4, 1960, pp 76-85.

8. Khesin, Ya. Ye. "Size of Nuclei and Functional State of Cells," Moscow, 1967.

9. Seregin, M. S., et al. in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 13, 1969, pp 78-93,

10. Lobova, T. M. KOSMICHESKAYA BIOL., No 5, 1973, pp 32-35.

11. Polenov, L. A. "Hypothalamic Neurosecretion," Leningrad, 1968.

12. Palkovits, M., and Fischer, J. "Karyometric Investigations," Budapest, 1968.

13. Koronakis, P., and Selye, H. in "Pressing Problems of General Pathology and Pathophysiology," Moscow, 1976, pp 27-48.

14. Gorizontov, P. D. in "Gomeostaz," Moscow, 1976, pp 428-458.

15. Meyerson, F. Z. "General Mechanism of Adaptation and Prevention," Moscow, 1973.

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REGIONAL REDISTRIBUTION OF RAT BLOOD AFTER 7 AND 30 DAYS OF HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
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[Article by O. A. Kovalev, V. F. Lysak, V. I. Severovostokova and S. K. Sheremetevskaya, submitted 28 Nov 78]

[English abstract from source]

An exposure of rats to hypokinesia was accompanied by a significant increase in the total amount of circulating blood per unit body mass. The percentage blood content was increased in the myocardium, lungs, liver, kidneys, small intestine, muscles and bones of the chest. The percentage blood content was decreased in the skin of different body segments, muscles and bones (except of the chest), tail, viscera (large intestine, adrenals, spleen, bladder, testes). The major regional redistribution of blood was its displacement into the liver.

[Text] The specific effect of "pure" hypokinesia can be studied in experiments on animals, the prolonged restriction of which is unrelated to changes in hydrostatic conditions.

We did not encounter publications in the literature accessible to us pertaining to the results of concurrent studies of absolute and relative fluctuations in filling of a rather large number of organs and tissues with blood under hypokinetic conditions. The only data published were obtained by morphological methods [1], which cannot be considered adequate to solve this problem. In this article, we describe the regional redistribution in circulating blood volume demonstrated with the use of radioisotopes in rats following 7 and 30 days of hypokinesia.

Methods

Experiments were conducted on nonanesthetized male rats weighing 180-200 g. The animals' appearance and behavior did not differ from normal. The rats were conditioned to the laboratory situation, they became used to the experiment and allowed themselves to be held. Four days prior to the experiment, we introduced a catheter into the external jugular vein of animals under mild hexenal anesthesia (5-7 mg/100 g weight, intraperitoneally). The catheter was inserted under the skin in the occipital part of the head, and it was flushed twice a day with sterile 0.9% sodium chloride solution with heparin. The rats became used to our handling the catheter by the time blood volumes had to be analyzed. They were kept on the standard laboratory diet. We made the studies on a fasting stomach (last feeding 18-20 h before the experiment), but without restricting water intake, in order to minimize scatter of data related to the possible influence of the digestion process.

To produce hypokinetic conditions, the animals were put in very small cages with the body in the usual position. The cages were made of plexiglas, and they restricted significantly voluntary movements in all directions. We conducted three series of tests to study regional redistribution of blood: the first and second series involved keeping the animals in the small cages for 7 and 30 days; the third series served as a control. We used 14 rats in each series.

Changes in regional blood volume were studied in the following manner: Intravenous injections were given to ^{51}Cr-labeled donor rat erythrocytes, as well as ^{131}I-labeled human serum albumins. The ratio of radioactivity of labeled formed elements to total activity of the tracer given to the animal equaled the value of individual blood hematocrit obtained when the tail was cut. The volume of injected tracer constituted 0.4 mℓ, and its total radioactivity was about 10 μCi. After uniform mixing of the tracer in the blood stream (10 min for labeled erythrocytes and 3 min for labeled plasma components), we induced cardiac arrest with an intravenous injection of 0.7 mℓ saturated KCl solution. The carcasses were frozen to -20°C for 2 h. Preparations were made of extracted organs and tissues to be studied. In each of the isolated specimens, we determined radioactivity, the level of which was proportionate to the amount of blood. We analyzed only differences between the control and experiment. There is evidence of the fact that the changes demonstrated by this method occurred before death, in spite of cardiac arrest induced by KCl [2].

Three series of experiments (11 rats in each) were conducted under analogous conditions to obtain the general characteristics of the model of hypokinesia. In these experiments, we measured pressure in the common carotid artery (AP) by the direct method, heart rate (HR) on the EKG, total circulating blood volume (TBV) by the method of dilution of ^{51}Cr-labeled erythrocytes and ^{131}I-labeled albumins. In addition to the parameters of systemic hemodynamics, we studied some parameters of carbohydrate metabolism, since impairment of the latter plays an important role in development of pathological changes under hypokinetic conditions [3]. We assayed lactic acid (LA), pyruvic acid (PA) content of blood, LA/PA ratio and lactic acid excess. We used conventional techniques [4, 5] to determine the parameters of carbohydrate metabolism.

When we analyzed the results, we evaluated the difference between mean values according to Student's *t* criterion. We used factor analysis in a modification that enabled us to supply a multidimensional description of changes between the control and experiment in order to characterize regional redistribution of blood [6]. We used an M-222 computer for statistical processing.

Results and Discussion

Table 1 lists the averaged values of parameters of systemic hemodynamics and carbohydrate metabolism for the control and experimental groups. The results are indicative of a statistically significant ($P<0.01-0.001$) increase in HR, TBV and appearance of lactic acid excess under the influence of hypokinesia. The changes in other parameters did not reach a level of statistical reliability. The increase in TBV (per unit weight) is consistent with data in the literature [7, 8]. This reaction was the opposite of the one demonstrated in other mammalian species and man, in which restricted motor activity induces a decrease in TBV [9].

Table 1. Some parameters of systemic hemodynamics and carbohydrate metabolism in hypokinetic rats

Parameter	Control	Hypokinesia				
		7 days		30 days		
	$M \pm m$	$M \pm m$	P_{1-2}	$M \pm m$	P_{1-3}	P_{2-3}
	1	2		3		
AP, mm Hg	121±2,20	124±3,10	>0,250	116±2,60	>0,100	>0,050
HR, per min	375±16,6	420±16,3	>0,050	464±14,2	<0,001	<0,010
TBV, mg/g weight	55±1,78	68±2,34	<0,001	73±4,36	<0,002	>0,500
Blood LA content, mmole/ℓ	1,86±0,26	2,54±0,32	>0,100	2,86±0,41	>0,050	>0,050
Blood PA content, mmole/ℓ	0,16±0,02	0,18±0,02	>0,250	0,17±0,03	>0,500	>0,500
LA/PA	11,6±1,42	14,1±1,46	>0,250	16,8±2,62	>0,050	>0,250
LA excess, nmole/ℓ	—	0,50±0,02	<0,001	0,90±0,05	<0,001	<0,001

On the whole, hypokinesia elicited relatively minor changes in parameters of systemic hemodynamics and carbohydrate metabolism. We failed to demonstrate significant metabolic disturbances that could have a marked local humoral effect on vascular tonus.

In view of the significant increase in TBV, the absolute blood content of all organs and tissues increased. Table 2 shows the significance of

Table 2. Changes in relative blood content (%TCB) in hypokinetic rat organs and tissues

Part of body	Tissues and organs	Control $M \pm m$	Rating, changes with hypokin.			
			7 days		30 days	
			P	f_1	P	f_1
Head	Skin	0,69±0,063	>0,500—	—0,337	>0,500+	—0,179
	Muscles and bones	3,68±0,292	>0,100—	—0,488	>0,250—	—0,402
	Brain	0,38±0,050	>0,500—	—0,218	>0,500+	—0,092
Neck	Skin	0,59±0,065	>0,250—	—0,302	>0,050—	—0,625
	Muscles and bones	2,76±0,258	>0,050—	—0,581	<0,020—	—0,625
Chest	Skin	1,27±0,123	>0,100—	—0,001	<0,010—	—0,385
	Muscles and bones	6,59±0,267	<0,002+	+0,024	<0,050+	+0,327
	Myocardium	1,60±0,154	<0,020+	+0,369	<0,050+	+0,593
	Lungs	7,60±0,579	0,050+	+0,161	<0.010+	+0,525
Abdomen and pelvis minor	Skin	1,63±0,278	>0,050—	—0,511	>0,050—	—0,458
	Muscles and bones	9,84±0,703	<0,001—	—0,595	<0,002—	—0,642
	Liver	36,1±1,227	<0,010+	+0,698	<0,050+	+0,536
	Small intestine	1,74±0,243	>0,250+	+0,255	<0,050+	+0,375
	Large intestine	1,56±0,134	<0,001—	—0,628	<0,001—	—0,687
	Stomach	0,70±0,097	>0,500+	+0,244	>0,500—	—0,050
	Kidneys	2,97±0,142	<0,020+	+0,479	>0,050+	+0,559
	Adrenals	0,10±0,011	<0,020—	—0,404	>0,100—	—0,259
	Spleen	3,84±0,843	<0,010—	—0,370	<0,002—	—0,578
	Pancreas	0,50±0,105	>0,500+	+0,162	>0,050—	—0,341
	Bladder	0,07±0,010	<0,001—	—0,534	<0,020—	—0,419
	Testes	1,38±0,100	>0,250—	—0,461	>0,100—	—0,362
Extremities: hind	Skin	0,37±0,069	>0,250—	—0,213	>0,500—	—0,194
	Muscles and bones	2,19±0,160	<0,001—	—0,642	>0,050—	—0,579
front	Skin	0,75±0,132	>0,100—	—0,258	>0,100—	—0,392
	Muscles and bones	3,26±0,319	>0,100—	—0,508	>0,500—	—0,323
	Tail	0,89±0,159	>0,250—	—0,530	>0,500	—0,212
Overall	Skin	5,32±0,348	<0,020—	—0,671	<0,002—	—0,772
	Muscles and bones	28,3±0,898	>0,250—	—0,662	>0,500—	—0,364
	Viscera	65,5±1,122	>0,100+	+0,765	>0,100+	+0,537
	Wt. of 1st factor, %	—	—	21,5	—	21,4
	Wt. of 2d factor, %	—	—	15,7	—	14,2

differences between mean values according to criterion t (P) and evaluation of factor load 1 (f_1). A "+" sign with the figures in the P and columns is indicative of relative increase in regional filling, as compared to the control, while a "-" sign is indicative of decrease. The factor load was statistically significant ($P<0.05$) with an absolute value of ≥ 0.360. Factor load 1 is a quantitative characterization of the degree of interrelation between changes in each vascular region and changes in all other examined parts of the blood stream for this factor. The contribution of factor load 1 to the overall evaluation of differences between the experiment and control was of decisive significance.

The results listed in Table 2 indicate the following: Hypokinesia induced redistribution of blood in the liver, heart (myocardium), lungs, kidneys, small intestine, muscular and osseous tissue of the chest. There was a decrease in percentile blood content of the skin, muscle and bone tissues (with the exception of the chest), tail, some viscera (large intestine, adrenals, spleen, bladder, testes). Evidently, the main direction of regional changes was determined by redistribution of blood in the liver, which contains the largest share of TBV, as compared to other parts of the blood stream.

Similar regional redistribution of blood, with predominant shift into the liver, was observed in cases of hemorrhage against the background of anesthesia or immobilization, at the early stage following trauma in the presence of moderate cooling, and with infusion of excessive amounts of donor blood [10]. All this enables us to consider the redistribution of blood in the liver under hypokinetic conditions to be a nonspecific reaction. This reaction may be related to generalized constriction of capacitive vessels under the influence of nonspecific stimulation of the parasympathetic nervous system and hypothalamo-hypophysea-adrenal system under the influence of various stress agents [11, 12]. Evidently, the physiological purpose thereof is to mobilize the intravascular dynamic reserve localized in capacitive vessels [13, 14]. The blood mobilized for more active circulation is redistributed in organs and tissues, the functional activity of which is relatively increased under hypokinetic conditions as a result of diminished tonus of skeletal muscles: heart, lungs and muscles of the chest, liver, kidneys, small intestine. Perhaps, mobilization of blood from capacitive vessels is supplemented with more marked constrictive influences on resistive vessels of some parts of the skin, skeletal muscles and some of the abdominal viscera, which could also be instrumental in the above-described redistribution of blood. The results of physiological studies, which indicated quantitative dissimilarity of neurogenic constrictive influences of various parts of the blood stream on resistive vessels, are also in favor of this interpretation [15, 16]. Evidently, special studies are needed to identify the mechanisms of regional redistribution of circulating blood under hypokinetic conditions.

BIBLIOGRAPHY

1. Portugalov, V. V.; Savina, Ye. A.; Kaplanskiy, A. S.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 4, 1976, pp 19-24.

2. Kovalev, O. A. PAT. FIZIOL. [Pathological Physiology], No 3, 1977, pp 84-87.

3. Petrova, N. V., and Portugalov, V. V. KOSMICHESKAYA BIOL., No 5, 1977, pp 66-72.

4. Marbach, E. R., and Weil, M. N. CLIN. CHEM., Vol 13, 1958, pp 244-271.

5. Huckabee, W. J. CLIN. INVEST., Vol 37, 1958, pp 244-271.

6. Kovalev, O. A.; Nopochatov, O. N.; and Kolodyazhnyy, S. F. "Multidimensional Evaluation of the Resluts of Clinical and Experimental Studies Using a New Method Based on Factor Analysis. Lecture on Pathophysiology for Physicians," Leningrad, 1978.

7. Vasil'yev, P. V.; Uglova, N. N.; Volozhin, A. I.; et al KOSMICHESKAYA BIOL., No 2, 1973, pp 13-173.

8. Krotov, V. P. "Kinetics and Regulation of Fluid-Electrolyte Metabolism in Hypokinetic Man and Animals," doctoral dissertation, Moscow, 1977.

9. Scholer, H. AM. HEART J., Vol 69, 1965, pp 701-712.

10. Kovalev, O. A. COR ET VASA (Prague), Vol 20, No 3, 1978, pp 230-238.

11. Chien, S. PHYSIOL. REV., Vol 47, 1967, pp 214-288.

12. Selye, H. AM. SCIENTIST, Vol 61, 1973, pp 692-699.

13. Folkow, B., and Mellander, S. AM. HEART J., Vol 68, 1964, pp 397-408.

14. Mason, D. T., and Bartter, P. C. ANESTHESIOLOGY, Vol 29, 1968, pp 681-692.

15. Khayutin, V. M. "Vasomotor Reflux [sic]," Moscow, 1964.

16. Tkachenko, B. I. in "Regionarnyye i sistemnyye vasomotornyye reaktsii" [Regional and Systemic Vasomotor Reactions], by B. I. Tkachenko, D. P. Dvoretskiy, V. I. Ovsyannikov et al., Leningrad, 1971, pp 257-270.

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SECRETION, INCRETION AND RESECRETION OF PANCREATIC LIPASE DURING PROLONGED RESTRICTION OF MOTOR ACTIVITY

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[Article by I. L. Medkova, N. M. Nikolayeva and K. V. Smirnov, submitted 22 Feb 79]

[English abstract from source]

The effect of 20, 60, 90 and 120-day hypokinesia on secretion, incretion and recretion of pancreatic lipase of rats was examined. It was found that 60, 90 and 120-day hypokinesia induced significant and similar changes — lipase decrease in the pancreas and increase in blood, bile, salivary glands and stomach mucosa; 20-day hypokinesia did not produce any effect on the above parameters.

[Text] In the last few years, new data have been obtained on the state of the digestive system in hypokinetic man and animals. Studies of man and animal experiments demonstrated changes in activity of a number of digestive enzymes responsible for hydrolysis of proteins, fats and carbohydrates [1-3]. Thus, activation of proteolytic enzymes and depression of carbohydrase activity were demonstrated under hypokinetic conditions of different duration. Yet there have been very few works published that deal with lipolytic enzymes when motor activity is restricted, and the information pertaining to activity of pancreatic lipase is fragmentary. However, there are indications that there is an increase in total lipid, cholesterol, β-lipoprotein and nonesterified fatty acid content of the blood under hypokinetic conditions [4-7]. Authors relate this process to mobilization of fat from the fat depots. In our opinion, this could also be the result of intensification of digestion of food fats in the gastrointestinal tract. It is known that the role of lipids as sources of energy in the body increases when motor activity is restricted and there is impairment of hydrolysis, transport and utilization of carbohydrates [4, 8].

Pancreatic lipase is the most important enzyme, which hydrolyzes chiefly long-chain triglycerides.

Pancreatic lipase is formed in acinar cells of the pancreas and passes with pancreatic juice into the duodenum, where the first stages of hydrolysis of alimentary fats occur. In addition, it passes into blood and lymph [9-17].

Pancreatic enzymes constantly circulate in the blood stream, and under normal physiological conditions their concentrations are maintained within a specific range [18-20]. This warrants reference to "exocrine-endocrine distribution" of products of secretory activity of the pancreas [21].

It is assumed that there is circulation of pancreatic enzymes between blood and the pancreas [22]. The enzymes entering the pancreas can then be resecreted with pancreatic juice [23]. It is believed that preservation of enzymes of pancreatic secretion by means of enteropancreatic circulation is important to preservation of energy for digestive processes.

The hypothesis has also been expounded that pancreated enzymes increted in blood may be significant to regulation of external secretory function of the pancreas, controlling synthesis and excretion of its enzymes by the feedback principle [16, 24]. In addition, the opinion is held that the physiological purpose of pancreatic enzymes that enter blood and lymph is involvement in interstitial metabolism [25, 26].

The level of lipolytic activity of blood depends primarily on the amount of lipase received from the pancreas, levels of excretion of lipase in urine, as well as resecretion ["recretion"] of the enzyme by different glands. In this case, recretion refers to the process of secretion of digestive enzymes from the blood by different organs, which are not producers of these enzymes. The recreted enzymes do not undergo appreciable conversions in the cell, and they are secreted in the same form as they came there. They can be involved in hydrolytic processes in the digestive tract [19, 20, 27]. Pancreatic lipase is resecreted by such glands as the gastric [19, 20, 28, 29], salivary [20, 29], intestinal [30, 31] and lactic [20].

Our objective here was to study secretion of pancreatic lipase by the pancreas, incretion thereof into blood and excretion of the enzyme by means of recretion by the salivary glands, glands of the stomach and liver as part of bile.

Methods

We conducted our studies on male, mongrel albino rats weighing 180-220 g. The animals were put in small, special hypokinetic cages for 20, 60, 90 and 120 days. We used 48 rats in all, 6 in the control and each experimental group. Cannulation of the common bile duct by the method used at the Institute of Nutrition, USSR Academy of Medical Sciences, was performed to obtain bile after hypokinesia. The animals were decapitated. We determined the activity of pancreatic lipase in blood serum, pancreatic tissue, gastric mucosa, salivary gland tissue and bile by the method of Myrtle and Zell [33] as modified by I. L. Medkova et al. [34]. This method was used to determine lipase activity, not only in blood, but other biological fluids and tissues. Studies of lipase activity in organs, tissues and media by the same method using the same substrate makes it possible to maintain that we are dealing with the activity of the same enzyme. We took 1 μmole of nonesterified fatty acids formed from the substrate per minute, scaled to 1 liter of blood serum, urine, bile or 1 g wet tissue of the pancreas, salivary glands or gastric mucosa, as the unit of lipase activity.

Results and Discussion

Restriction of the animals' motor activity for 20 days had virtually no effect on activity of pancreatic lipase. We only demonstrated a tendency toward increase in enzyme activity in blood serum, salivary gland tissue, gastric mucosa and bile against the background of an unreliable decline of activity in pancreatic tissue (see Table). Longer restriction of movement (60 days) induced marked changes in secretion and incretion of lipase, secretion thereof by the gastric mucosa and salivary glands, and with bile. On the 60th experimental day, there was a reliable decrease in lipase activity in pancreatic tissue. At this time its level in blood almost tripled. There was also reliable increase in secretion of lipase by salivary glands and in bile. Significant changes in recretion of lipase were noted in the gastric mucosa. Its activity was more than 20 times higher than the base level (see Table).

On the 90th day of hypokinesia, the changes in activity of pancreatic lipase in the above-mentioned organs presented the same dynamics as with 60 days of immobilization, but less marked. There was a reliable decrease in lipase activity in pancreatic tissue. However, incretion thereof, as well as content in the gastric mucosa and salivary glands, increased less significantly than in the case of 60-day hypokinesia. There was a reliable increase in secretion thereof with bile.

On the 120th day of hypokinesia, we demonstrated a reliable decrease in pancreatic lipase activity in pancreatic tissue, whereas its activity in blood serum almost doubled, as compared to the control level. There was an increase in secretion of pancreatic lipase by the salivary glands and with bile. Lipase activity increased to 1.71±0.19 units in the gastric mucosa, as compared to the control (0.51±0.21 units; $P<0.01$), which corresponds to almost threefold increase in recretion thereof by this part of the stomach.

Activity (in units) of pancreatic lipase (M±m) in different biological media with 20, 60, 90 and 120-day restriction of motor activity

Day of hypokinesia	Pancreatic tissue		Blood serum	
	control	experiment	control	experim.
20	3808,0±219.76	3731,0±284,53	99,4±20,19	102,2±9,80
60	8551,2±416.25	4292,4±442,98***	118.56±33,45	312,6±25,28***
90	6202,0±375,29	3304,0±391,4***	164,64±14,44	195.3±7,88
120	7462,0±411,75	6090,0±257,31*	132,3±19,3	279,23±23,35**

	Gastric mucosa		Salivary gland tissue		Bile	
	control	experim.	control	experim.	control	experim.
20	0.98±0,42	1,46±0,45	0,2±0,068	0,22±0,1	504,0±73,95	554,0±121,3
60	0,01±0,0	0,202±0,016***	0,72±0,166	1,1±0,183	563,5±84,79	1186,5±149,26***
90	0,73±0,27	0,95±0,21	0,97±0,112	1,42±0,197	385,0±60,78	668,0±67,22**
120	0,51±0,21	1,71±0,19**	0,91±0,11	1,23±0,12	637,0±111,34	1008.0±115,28*

*P<0.02 (as compared to control) ***P<0.001
**P<0.01

Thus, the submitted results indicate that 20-day hypokinesia has virtually no effect on synthesis of pancreatic lipase, secretion thereof into blood and various digestive glands. Hypokinesia for 60, 90 and 120 days elicits significant changes, in the same direction, in lipase activity: reliable decrease in pancreatic tissue, significant increase in blood and redistribution in organs; intensified secretion by the gastric mucosa, salivary glands and with bile. The most profound changes occur with 60- and 120-day hypokinesia. The demonstrated correlation between secretion of lipase by various digestive glands and level thereof in blood is indicative of the recretory origin of the enzyme in these glands.

We did not consider all possible routes of elimination of the enzyme in our experiments. However, our findings are consistent with existing conceptions [19, 20, 29, 34] that enzymatic homeostasis of blood is provided by balanced incretion, as well as levels of renal and extrarenal excretion of the enzyme from the body.

As can be seen from the submitted data, high blood lipase levels on the 60th, 90th and 120th day of hypokinesia were associated with a reliable decrease in its activity in pancreatic tissue. We assume that this may indicate intensified exosecretion of the enzyme into the duodenum against the background of normal synthesis thereof in the pancreas, on the one hand, and impairment of homeostatic function of the liver, when the enzyme level rises drastically in blood, while mechanisms of excretion and inactivation thereof are not adequately correlated, on the other hand.

The increase in pancreatic lipase content of digestive glands, which are not the sites of its synthesis, is a purposeful process directed toward stabilizing hydrolase level in peripheral blood serum and creation of optimum conditions for the most complete hydrolysis of lipids under hypokinetic conditions.

BIBLIOGRAPHY

1. Smirnov, K. V. "Activity of the Digestive System During Exposure to Space Flight Factors," doctoral dissertation, Moscow, 1973.
2. Potemkina, L. S.; Goland, L. G.; Murashko, V. V.; et al. in "Fiziologiya i patologiya organov pishchevareniya" [Physiology and Pathology of Digestive Organs], Moscow, 1971, p 406.
3. Smirnov, K. V.; Goland, L. G.; Medkova, I. L.; et al. FIZIOLOGIYA CHELOVEKA [Human Physiology], No 4, 1976, p 653.
4. Lobova, T. M. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1973, p 32.
5. Parin, V. V.; Krupina, T. N.; Mikhaylovskiy, G. P.; et al. Ibid, No 5, 1970, p 59.
6. Bychkov, V. P.; Borodulina, I. I.; Gryaznova, V. N.; et al. in "Trudy 5-kh chteniy, posvyashchennykh razrabotke nauchnogo naslediya i razvitiyu idey K. E. Tsiolkovskogo. Sektsiya 'Problemy kosmicheskoy biologii'" [Transaction of 5th Lecture Series Dedicated to Development of the Scientific Legacy and Ideas of K. E. Tsiolkovskiy. Section on Problems of Space Biology], Moscow, 1971, p 132.
7. Goland, L. G. "Enzyme Secreting Function of the Pancreas During Exposure to Some Space Flight Factors," author abstract of candidatorial dissertation, Moscow, 1970.
8. Lobova, T. M., and Chernyy, A. V. KOSMICHESKAYA BIOL., No 6, 1977, p 36.
9. Boldyrev, V. N. RUSSK. VRACH [Russian Physician], No 2, 1914, p 45.

10. Milyushkevich, G. F. in "Nauchnaya konf. po problemam fiziologii i patologii pishchevareniya, posvyashchennaya pamyati akad. K. M. Bykova. Trudy" [Proceedings of Scientific Conference on Physiology and Pathology of Digestion Dedicated to the Memory of Academician K. M. Bykov], Ivanovo, 1960, p 547.

11. Dzhakson, I. M. "Exocrine Function of the Pancreas and Its Involvement in Regulation of Some Aspects of Metabolism," author abstract of doctoral dissertation, Leningrad, 1964.

12. Protsenko, V. A. "Effect of the Pancreas and Some Organs on Lipolytic Activity of Blood, Urine and Intestinal Juice," author abstract of candidatorial dissertation, Donetsk, 1964.

13. Kochnev, O. S., and Sharafislamov, F. Sh. in "Voprosy klinicheskoy khirurgii" [Problems of Clinical Surgery], Kazan', 1969, p 79.

14. Bartos, V.; Brzek, V.; and Groh, J. AM. J. MED. SCI., Vol 252, 1966, p 31.

15. Vega, R. E.; Appert, H. E.; and Howard, J. M. ANN. SURG., Vol 166, 1967, p 995.

16. Laporte, J.-C., and Tremolieres, J. C. R. ACAD. SCI. (Paris), Vol 273D, 1971, p 1205.

17. Papp, M., et al. EXPERIENTIA, Vol 33, 1977, p 1191.

18. Ugolev, A. M.; Iyezuitova, N. N.; Masevich, Ts. G.; et al. "Studies of the Human Digestive System," Leningrad, 1969.

19. Korot'ko, G. F. "Excretion of Enzymes by Gastric Glands," Tashkent, 1971, p 18.

20. Abdurakhmanov, Kh. Kh.; Vepritskaya, E. A.; Glushko, L. F.; et al. in "Vsesoyuznoye fisiologicheskoy o-vo im. I. P. Pavlova. S"yezd. 12-y. Referaty dokladov na simpoziumakh" [Abstracts of Papers Delivered at Symposiums of the 12th Congress of the All-Union Physiological Society imeni I. P. Pavlov], Leningrad, Vol 1, 1975, p 233.

21. Janowitz, H. D., and Hollander, F. GASTROENTEROLOGY, Vol 17, 1951, p 591.

22. Thomas, J. E. MED. CLIN. N. AMER., Vol 40, 1956, p 273.

23. Gotze, H., and Rothman, S. S. NATURE, Vol 257, 1975, p 607.

24. Leibow, C., and Rothman, S. S. SCIENCE, Vol 189, 1975, p 472.

25. Kretovich, V. L. "Introduction Into Enzymology," Moscow, 1967.

26. Dumont, A. E.; Doubilet, H.; and Mulholland, J. H. ANN. SURG., Vol 152, 1960, p 403.

27. Hirsch, J. C. in "Handbuch der Allgemeinen Pathologie," Berlin, Vol 2, No 1, 1955, p 92.

28. Inamova, K. B. "Amylase and Lipase in Secretions of Pyloric and Fundal Gastric Glands, and Possible Recretory Origin Thereof," author abstract of candidatorial dissertation, Tashkent, 1970.

29. Kamakin, N. F.; Abdurakhmanov, Kh. Kh.; Inamova, K. B.; et al. in "Mekhanizmy povrezhdeniya, rezistentnosti, adaptatsii i kompensatsii" [Mechanisms of Injury, Resistance, Adaptation and Compensation], Tashkent, Vol 2, 1976, p 34.

30. Gulyamov, T. K. "Compensatory and Adaptational Changes in the Small Intestine Under Different Functional Conditions," author abstract of doctoral dissertation, Tashkent, 1974.

31. Pulatov, A. S., and Glushko, L. F. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 3, 1977, p 452.

32. Korot'ko, G. F., and Kurzanov, A. N. Ibid, No 1, 1978, p 81.

33. Myrtle, J. F., and Zell, W. J. CLIN. CHEM., Vol 21, 1975, p 1469.

34. Medkova, I. L.; Smirnov, K. V.; Mazo, V. K.; et al. LABOR. DELO [Laboratory Record], No 3, 1978, p 142.

UDC: 612.227.3

THEORETICAL ANALYSIS OF THE EFFECT OF STATE OF PULMONARY CIRCULATION ON DISTRIBUTION OF VENTILATION-PERFUSION RELATIONS AND GAS EXCHANGE IN THE LUNGS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 68-71

[Article by A. I. D'yachenko and V. G. Shabel'nikov, submitted 24 Aug 79]

[English abstract from source]

Using a mathematical model of functionally nonuniform lungs, the effect of gravitational inequality of ventilation-perfusion relations on gas exchange was studied. The dependence of tensions of respiratory gases in the mixed arterial blood and alveolar air upon pulmonary circulation pressure was demonstrated. The influence of changes in the tone of lung vessels on the distribution of ventilation-perfusion relations and gas exchange was investigated.

[Text] As shown by experimental studies [1-3], the hemodynamic parameters of the pulmonary circulatory system have a substantial effect on degree of functional heterogeneity of the lungs. In particular, it was established that there is a marked correlation between arterioalveolar difference for carbon dioxide tension, which characterizes nonuniformity of ventilation-perfusion relations ($\dot{V}_A/\dot{Q}$) in the lungs, and pressure in the pulmonary artery [1]. Since the mechanism that determines this correlation is not quite understandable, our objective here was to make a quantitative study thereof by means of a mathematical model of functionally heterogeneous lungs, which was developed previously [4]. Our results enable us to assess the influence of possible changes in tonus of pulmonary vessels and blood pressure in them as a result of prolonged exposure to weightlessness on distribution of $\dot{V}_A/\dot{Q}$ and exchange of gases.

Methods

The mathematical model of functionally heterogeneous lungs consisted of three parts: models of blood flow, ventilation and gas exchange.

The blood flow model is based on analysis of the mechanics of stationary flow of liquid in an elastic vascular channel with proper dichotomic branching. Seven sections of the vascular bed are considered: 1) arterial reservoir; 2) extraalveolar arteries; 3) alveolar arteries; 4) capillaries; 5) alveolar veins; 6) extraalveolar veins; 7) venous reservoir. The resistance in sections 1 and 7, which are outside the pulmonary lobes, is considered as equal to zero. Blood pressure in them is hydrostatic. To describe the area of vascular cross section as a function of transmural pressure, we used approximation of empirical data [5, 6]. The equations for quasi-one-dimensional flow, written down for each section in a pulmonary lobe, were submitted to analytical integration. We obtained a system of equations which related blood flow Q, resistance of unstretched vessels R_i, elasticity of vessels α_i, and pressure at the start and end of the ith section. The equations describe vascular collapse with negative transmural pressure and stretching with positive transmural pressure.

We considered only nonuniformity of ventilation and blood flow due to +1 Gz acceleration. The lungs were divided into 10 horizontal layers. We numerically solved a system of equations describing blood flow and euqations of mechanics of pulmonary parenchyma [4] to calculate blood flow and ventilation in each layer.

Studies of the model of parenchymal mechanics revealed that the distribution of ventilation is related to blood volume in the lungs and changes therein in the course of a respiratory cycle. Thus, the hemodynamic parameters influence distribution not only of blood flow, but ventilation. This influence is more marked with increase in elasticity of the lungs and nonlinearity of the volume-transpulmonary pressure curve. In this study we used a slightly nonlinear volume-transpulmonary pressure curve for lungs with low elasticity [stretchability]. For this reason, the distribution of ventilation changes little with change in state of pulmonary circulation.

Using the calculated values of ventilation and blood flow, we numerically solved equations describing "ideal" exchange of gases [7] in each horizontal layer of the lungs. We used algorithms [8] to describe the link between concentrations of respiratory gases and their tension in blood. We calculated the gas composition of mixed arterial blood and mixed alveolar air, as well as ΔP_G: alveolar-arterial differences for oxygen tension ΔPO_2 and for carbon dioxide tension ΔPCO_2. Oxygen tension in venous blood was considered to be 40 mm Hg and that of carbon dioxide 45 mm Hg, i.e., we considered conditions of rest, tissular normoxia and normocapnia.

Results and Discussion

Tension of respiratory gases in blood and mixed alveolar air is related not only to nonuniformity of $\dot{V}_A/\dot{Q}$, but to the mean $\dot{V}_A/\dot{Q}$. A study was made of the effect on gas exchange of an increase in mean $\dot{V}_A/\dot{Q}$ with constant distribution of $\dot{V}_A/\dot{Q}$ in relation to the mean, which corresponded to moderate voluntary hyperventilation. The estimates made for different gravitational nonuniformities of $\dot{V}_A/\dot{Q}$ revealed that with increase of mean $\dot{V}_A/\dot{Q}$ from 0.85 to 1.5, ΔPO_2 decreases by about 40%, while ΔPCO_2 increases by less than 0.2 mm Hg. For a stationary state at rest, mean $\dot{V}_A/\dot{Q}$ equals 0.85-1.0 [2, 3]. We also submit the results obtained for a mean $\dot{V}_A/\dot{Q}$ of 0.85, since in this case the influence of nonuniformity of $\dot{V}_A/\dot{Q}$ on gas exchange is at a maximum. Analysis of the model revealed that with a constant mean $\dot{V}_A/\dot{Q}$ the distribution of $\dot{V}_A/\dot{Q}$ does not depend on overall resistance of unstretched vessels R_T, but on R_i/R_T ratios.

We selected "normal" values of R_i and α_i on the basis of previously published data [5, 6, 9]. In accordance with the results obtained in [10], let us consider that a change in tonus of arterial vessels leads to a change in R_2 and R_3 with constant α_2 and α_3. According to the model equations, there is virtually no change in distribution of $\dot{V}_A/\dot{Q}$ when pressure in the arterial and venous reservoirs is constant. Consequently, a change in vascular tonus could affect gas exchange only if there is a change in pressure in the pulmonary circulation, in arteries (P_V) and veins (P_V).

We calculated distribution of $\dot{V}_A/\dot{Q}$ and gas exchange with different levels of mean pressure in the main pulmonary artery and pulmonary veins in the case of "diminished tonus" of arterial vessels (R_2 = 9 mm Hg/cm^3/s, R_3 = 8 mm Hg/cm^3/s) and "normal" other R_i, α_i. A comparison of the estimates made for "normal" and "diminished" tonus revealed that the ΔP_G gradient constitutes a few percentage points with the same pressure in the pulmonary circulation.

Figure 1 illustrates estimated and experimental curves of distribution of $\dot{V}_A/\dot{Q}$ over the height of the lungs. Figure 1 shows that the wide variability of the curves observed in our studies could be due to the difference in pulmonary artery pressure.

Figure 2 illustrates the effect of pressure changes in the pulmonary artery on exchange of gases. Estimates were made for a constant arteriovenous pressure gradient of 7.5 mm Hg. Figure 2 shows that CO_2 tension of arterial blood undergoes negligible change. ΔPCO_2 changes due to change in CO_2 tension in mixed alveolar air. This is consistent with experimental findings [1]. For oxygen, the opposite results are observed: ΔPO_2 changes more due to change in oxygen tension in arterial blood.

Figure 3 illustrates the influence of pressure in pulmonary veins and arteries on ΔP_G. We see that when pressure in the pulmonary circulation is high, and the lungs are entirely under the conditions of the third zone, ΔP_G is low. With decrease in pressure in the veins there is an increase in size of the second zone, and with decrease in pressure in the main pulmonary artery (P_a^0) the first zone increases, which increases ΔP_G. ΔPCO_2 as a function of pressure in the main pulmonary artery was obtained [1] for accelerations of +1 Gx with the following regression equation:

$$\Delta PCO = (11.9 - 0.54 \cdot P_a) \text{ mm Hg}.$$

In spite of the difference in position of the body, there is a conformity between theoretical and experimental data.

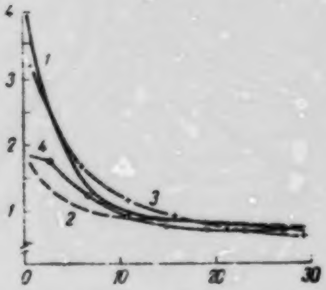

Figure 1.
Distribution of $\dot{V}_A/\dot{Q}$ over height of lungs. X-axis, distance from lung apices (cm); y-axis, $\dot{V}_A/\dot{Q}$
1, 2) theoretical curves
3, 4) experimental curves [2, 3]
For curve 1, blood pressure in common pulmonary artery is 16.5 mm Hg and pressure in pulmonary veins (left atrium) is 5.2 mm Hg. For curve 2, the respective pressures are 19.5 and 8.2 mm Hg. The distance between common pulmonary artery and veins to apices of the lungs is considered to be 18 cm.

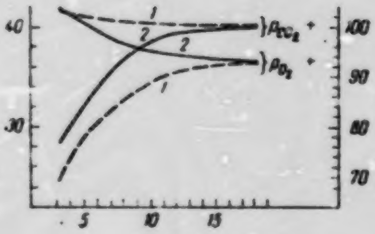

Figure 2.
Tension of respiratory gases in mixed arterial blood (1) and mixed alveolar air (2) as theoretical function of blood pressure in pulmonary artery; the "+" signs refer to "ideal lungs" [7]. X-axis, pressure in common pulmonary artery (mm Hg); y-axis; CO_2 tension (mm Hg) on the left and O_2 tension (mm Hg) on the right

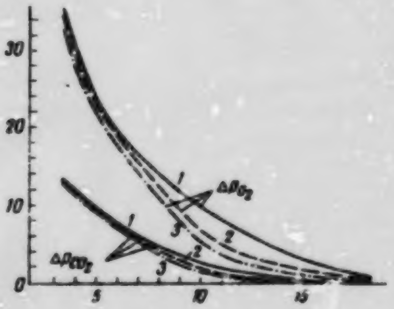

Figure 3.
ΔP_G as a theoretical function of blood pressure in common pulmonary artery. X-axis, blood pressure in common pulmonary artery (mm Hg); y-axis, ΔPO_2 and ΔPCO_2 (mm Hg).
1-3) arteriovenous blood pressure gradient of 11.3, 7.5 and 6 mm Hg

Blood pressure in the left atrium must be higher than in the lower part of the pleural cavity, i.e., over 2 mm Hg. At rest, blood flow through the lungs is at least 4 liters/min. Since $R_T > 100$ mm Hg/cm^3/s, pressure in the main pulmonary artery must be over 5 mm Hg. Consequently, Figure 3 illustrates the maximum effect of gravitational nonuniformity on ΔP_G. In addition to gravity, there may be other causes of nonuniformity of $\dot{V}_A/\dot{Q}$, as well as an anatomical shunt, which increases ΔP_G [11]. However, in healthy lungs at rest, gravity is the chief cause of nonuniformity of $\dot{V}_A/\dot{Q}$ [1-3, 11].

If vascular tonus is constant over the height of the lungs, exchange of gases is determined by pressure in the pulmonary circulation and depends little on vascular tonus. But if complete blood flow and $P_a - P_v$ remain constant with diminished tonus, the pressure in the pulmonary artery drops. This causes an increase in nonuniformity of $\dot{V}_A/\dot{Q}$ and ΔP_G. The question of quantitative changes in blood flow and pressure in the pulmonary circulation is beyond the scope of the model, since these changes depend on the state of systemic circulation. It must be noted that while a change in tonus leads to a change in α_i, distribution of $\dot{V}_A/\dot{Q}$ and exchange of gases change with constant pressure in the pulmonary circulation.

BIBLIOGRAPHY

1. Askrog, V. J. APPL. PHYSIOL., Vol 21, 1966, pp 1299-1306.
2. West, J. B. Ibid, Vol 17, 1962, pp 893-898.
3. Harf, A.; Pratt, T.; and Hughes, J. M. B. Ibid, Vol 33, 1978, pp 115-123.
4. Genin, A. M.; D'yachenko, A. I.; and Shabel'nikov, V. G. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow--Kaluga, Pt 1, 1979, pp 37-39.
5. Maloney, J. E.; Rooholamini, S. E.; and Wexler, L. MICROVASC. RES., Vol 2, 1970, pp 1-12.
6. Shapiro, A. M. TRANS. ASME, Vol K99, 1977, pp 126-147.
7. Rahn, H., and Fenn, W. O. "A Graphical Analysis of the Respiratory Gas Exchange (The O_2-CO_2 Diagram)," Washington, 1956.
8. Kelman, G. R. RESP. PHYSIOL., Vol 3, 1967, pp 111-115.
9. Milnor, W. R. in "Cardiovascular Fluid Dynamics," London, Vol 2, 1972, pp 299-340.

10. Ayvar, Yu. P., and Kalnin'sh, I. Ya. in "Vsesoyuznaya konf. po problemam biomekhaniki. 2-ya" [Second All-Union Conference on Problems of Biomechanics], Riga, Vol 1, 1979, pp 149-151.

11. Gledhill, N.; Froese, A. B.; Buick, F. J.; et al. J. APPL. PHYSIOL., Vol 45, 1978, pp 512-515.

METHODS

UDC: 629.78:658.311.44]:[616.12-008.3+616.831-005]-036.15-072.7

METHOD FOR ASSESSING HEMODYNAMICS AND DETECTING LATENT INSUFFICIENCY OF CEREBRAL CIRCULATION IN COSMONAUT CANDIDATES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 71-74

[Article by D. A. Alekseyev, submitted 9 Nov 78]

[Text] Experience in screening cosmonaut candidates shows that many of them present osteochondrosis of the cervical spine. In some of the selected individuals, the signs of intervertebral osteochondrosis are progressing. Osteophytes in this region sometimes cause ischemic circulatory disturbances in the vertebrobasilar system as a result of reflex angiospasm of vertebral arteries and mechanical compression of the latter [1-4]. For this reason, in expert screening of this group of candidates, it is very important to assess blood flow in the systems of the vertebral arteries (basilar and internal carotid), determine the functional capabilities of collaterals and latent circulatory disturbances in the corresponding vascular reservoirs. A functional test is used for this purpose, involving rotation of the head and throwing it back to an angle of 45° [5-10].

Methods

Cosmonaut candidates with osteochondrosis of the cervical spine (28 people ranging in age from 23 to 44 years) and 15 healthy volunteers 25-37 years of age (control group) rotated their head to the side to the maximum degree and threw it back to an angle of 45°. We recorded the EEG from 8 symmetrical points of the scalp (forehead, center, temple and occiput) synchronously with the REG [rheoencephalogram] (frontomastoid and occipitomastoid leads). Synchronous recording of the REG and EEG enabled us to determine the correlation between degree of decrease in delivery of blood to the brain and cerebral hypoxia that occurred [1, 7, 9, 11].

Results and Discussion

There was appreciable decrease in amplitude of the occipitomastoidal REG by 19.2-20.6% ($P<0.05$) on the side of the turn when individuals with cervical osteochondrosis turned their head to the sides. When the head was thrown back, the reduction of pulsed delivery of blood to the basins of the vertebral and basilar arteries reached 23.1-27.3% ($P<0.001$), as compared to the background. These changes were less marked in the basin of the internal carotid artery (Figure 1). The decreased pulsed filling of cerebral vessels while turning the head and throwing it back was associated with significant adaptational redistribution of tonus of arteries and veins with large, medium and small caliber, most marked in the basin of the internal carotid, in individuals with early manifestations of osteochondrosis.

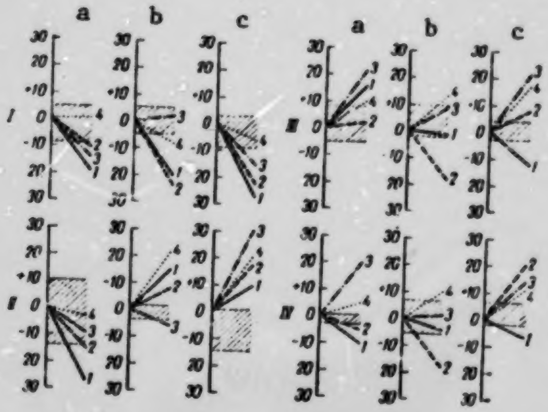

Figure 1. Dynamics of mean values of REG parameters (% of base levels) while turning the head and throwing it back, in individuals with early manifestations of cervical osteochondrosis. Striped areas show the range of fluctuation of REG parameters during functional tests on the control group of subjects

I) maximum REG amplitude
II) index α/T
III) diastolic index
1, 2) right and left occipitomastoidal REG
3, 4) right and left frontomastoidal REG
a) turn to the right
b) turn to the left
c) head thrown back

There was particularly significant increase in tonus of arteries and veins of different caliber when the head was thrown back, and this is apparently related to overstimulation of the vertebral nerve and cervical sympathetic plexus by the osteophytes [12-14]. The nitroglycerin test confirmed the predominantly reflex genesis of increased cerebrovascular tonus in individuals with osteochondrosis: under the influence of nitroglycerin

(0.00025 under the tongue) turning or throwing the head back no longer caused a decrease in pulsed delivery of blood or change in tonus of cerebral vessels. However, in some subjects, the deficient pulsed filling of the vertebrobasilar system on the side of the turn and when the head was thrown back persisted even with intake of nitroglycerin, and this was indicative of prevalence of mechanical effect of osteophytes on the vascular wall.

The most marked changes in dominant rhythm on the EEG were observed when the head was thrown back: appreciable increase in amplitude and index of α-rhythm, smoothing of zonal differences (Figure 2). These changes in the direction of hypersynchronization of bioelectrical activity when the head was turned and particularly when it was thrown back occurred in all subjects with early signs of cervical osteochondrosis and in eight subjects in the control group.

In addition, in 7 subjects with early manifestations of cervical osteochondrosis we observed appreciable increase in number of low-amplitude (to 35 μV) diffuse θ- and δ-waves on the EEG, against the background of decreased amplitude of dominant rhythm, i.e., "flattening" of the EEG, when turning the head in the direction of greatest decrease in pulsed filling (to 36% of the base level), i.e., of maximum deterioration of patency of the vertebral artery, as well as when the head was thrown back. Along with background α-activity, we recorded segments of low-amplitude (40-60 μV) slow (7-8 Hz) α-rhythm (Figure 3). Such EEG changes were not observed in the control group of subjects.

The decreased amplitude and index of dominant rhythm, as well as in diffuse low-amplitude slow activity on the EEG, were observed by V. A. Chukhrova in the presence of brief circulatory hypoxia [7].

Consequently, the observed synchronous changes in the REG and EEG during the functional test (appearance of moderate, diffuse changes in bioelectrical activity of the brain following appreciable decrease in pulsed delivery of blood to the vertebrobasilar system) are indicative of the circulatory ischemic nature of the above-mentioned electroencephalographic changes in subjects with early signs of cervical osteochondrosis. This is also confirmed by the appearance of reactive cerebral hyperemia immediately after the test involving tilting the head back. As we know, reactive hyperemia occurs in response to prior ischemia of cerebral tissue [15, 16]. Since this group of subjects had no subjective or objective clinical manifestations of disease, we could only be dealing with detection of latent insufficiency of circulation, inadequate delivery of blood to the vertebrobasilar system as a result of insufficient effectiveness of collateral circulation with the use of these functional tests (which temporarily limit blood flow to the vertebral arteries).

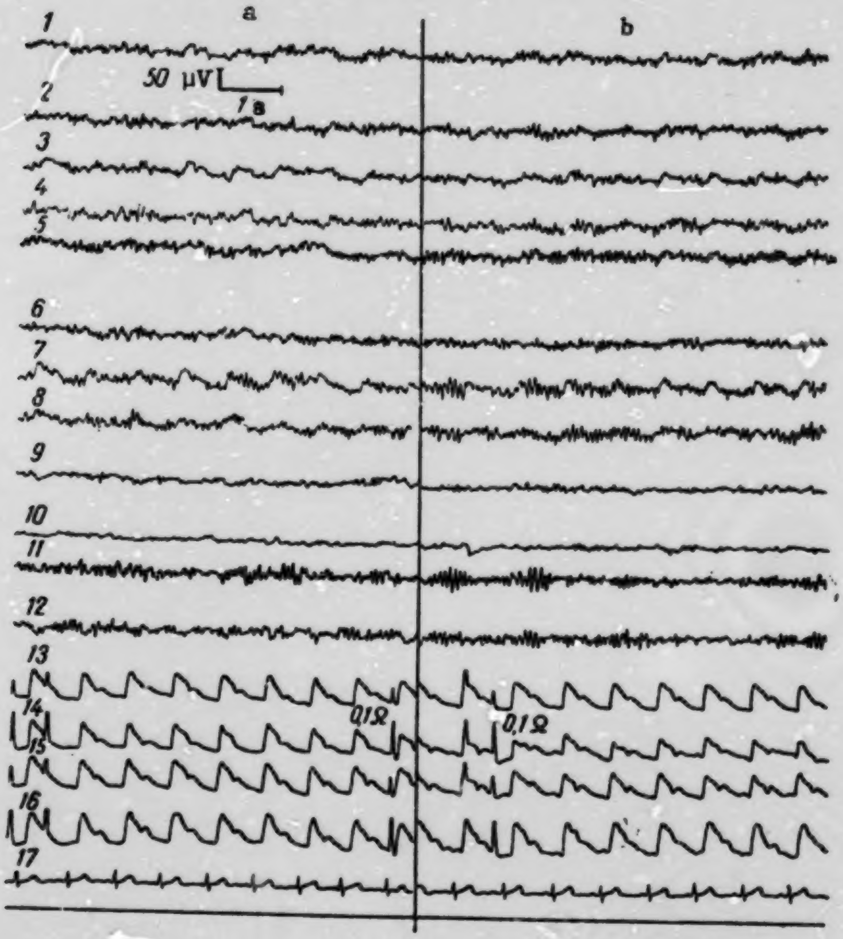

Figure 2. EEG and REG of subject S., 45 years old, with early signs of cervical osteochondrosis, before (a) and while (b) throwing the head back. When the head is thrown back there is significant decrease in maximum amplitude of the right occipito-mastoidal REG associated with some increase in amplitude and index of dominant EEG activity

Here and in Figure 3:

1, 2) right and left frontal monopolar EEG leads (silent electrode on the ear)
3, 4) right and left central leads
5, 6) right and left temporal leads
7, 8) right and left occipital leads
9, 10) right and left fronto-central bipolar EEG leads
11, 12) right and left central occipital bipolar EEG leads
13, 15) right and left fronto-mastoidal REG leads
14, 16) right and left occipito-mastoidal REG leads
17) EKG (first standard lead)

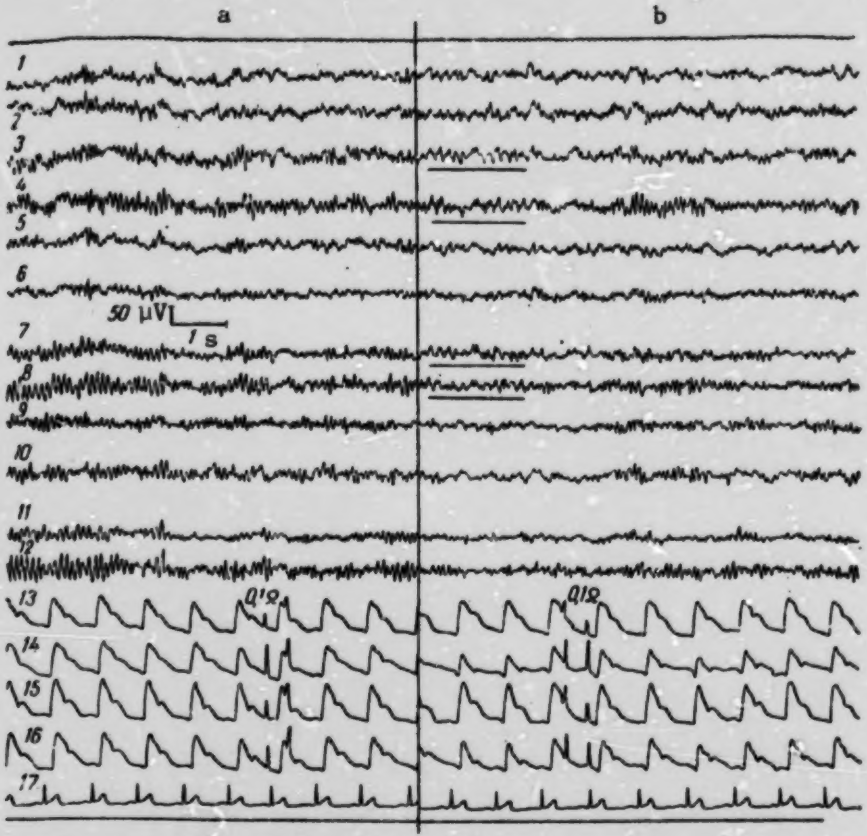

Figure 3. EEG and REG of subject M., 37 years old, with early signs of cervical osteochondrosis, before (a) and while (b) throwing the head back. While throwing the head back there is a significant decrease in maximum amplitude of the right and left occipitomastoidal REG (decreased pulsed delivery of blood to the vertebral and basilar arteries), appearance of groups of low-amplitude, polymorphic slow waves (underlined), against the background of decreased amplitude, index and slowing of main rhythm

Since ischemic reactions appear on the EEG of individuals with early signs of cervical osteochondrosis only when the supply of blood comes close to a critical level [4, 6, 7, 9, 17], a decrease in pulsed delivery of blood to the basin of the vertebral and basilar arteries to less than 30% of the base level on the side of the head turn and when it is thrown back, against the background of appearance of slow EEG activity, can be considered an important criterion of latent circulatory insufficient of the vertebral and basilar system.

Thus, synchronous recording of the REG and EEG during functional tests involving head turning and throwing the head back before and during the effect of nitroglycerin has acquired importance for expert certification, since it permits not only determination of the state of cerebral hemodynamics, but detection of latent circulatory insufficiency in the vertebrobasilar system in individuals with early signs of osteochondrosis of the cervical spine.

BIBLIOGRAPHY

1. Yarullin, Kh. Kh. in "Klinicheskaya neyrofiziologiya" [Clinical Neurophysiology], Leningrad, 1972, pp 544-559.
2. Shmidt, Ye. V. ZH. NEVROPATOL. I PSIKHIATR. [Journal of Neuropathology and Psychiatry], No 12, 1973, pp 1761-1771.
3. Vereshchagin, N. V. in "Sosudistyye zabolevaniya nervnoy sistemy" [Vascular Disease of the Nervous System], edited by Ye. V. Shmidt, Moscow, 1975, pp 398-416.
4. Boismare, F., and Boquet, J. SEM. HOP. PARIS, Vol 50, 1974, pp 819-825.
5. Kunert, W. Z. KREISL.-FORSCH., Vol 50, 1961, pp 572-580.
6. Yarullin, Kh. Kh. "Clinical Rheoencephalography," Leningrad, 1967.
7. Chukhrova, V. A. "Functional Electroencephalography in the Presence of Lesions to Great Vessels of the Head," Moscow, 1973.
8. Eninya, G. I. "Rheography as a Technique for Assessing Cerebral Circulation," Riga, 1973.
9. Ginzburg, S. Ye. "Electrical Activity and Hemodynamics of the Brain With Occlusion of Cerebral Arteries," Minsk, 1974.
10. Lebedeva, L. I. in "Metody klinicheskoy neyrofiziologii" [Methods of Clinical Neurophysiology], Leningrad, 1977, pp 40-66.
11. Alekseyev, D. A. "Regional Hemodynamics With the Use of Different Intensities of Antiorthostatic Factors," author abstract of candidatorial dissertation, Moscow, 1974.
12. Yarullin, Kh. Kh., and Tabeyeva, D. M. in "Aktual'nyye voprosy nevropatologii" [Pressing Problems of Neuropathology], Alma-Ata, 1971, pp 54-56.

13. Brotman, M. K. in "Osteokhondroz pozvonochnika" [Osteochondrosis of the Spine], Novokuznetsk, Pt 1, 1973, pp 15-22.

14. Nagulic, J., et al. VOJNOSANIT. PREGL., Vol 32, 1975, pp 8-14.

15. Konradi, G. P. "Regulation of Vascular Tonus," Leningrad, 1973, p 177.

16. Zimmer, R.; Lang, R.; and Oberdorster, G. PFLUG. ARCH. GES. PHYSIOL., Vol 328, 1971, pp 332-343.

17. Ingvar, D. H.; Sjolund, B.; and Ardo, A. ELECTROENCEPH. CLIN. NEUROPHYSIOL., Vol 41, 1976, pp 268-276.

UDC: 616.14-005.741.9-073.432.19

ULTRASONIC METHOD OF RECORDING GAS BUBBLES IN ANIMAL VENOUS BLOOD IN A RAREFIED ATMOSPHERE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 74-76

[Article by R. T. Kazakova, submitted 15 May 78]

[Text] Since 1968, there have been descriptions published of a method of recording [demonstrating] intravascular gas bubbles, which appeared under the influence of decompression due to elevated pressure, with the use of ultrasonic equipment [1-4]. With this method, it was possible to determine that the presence of gas bubbles in blood is not necessarily associated with clinical symptoms, and that bubbles may appear long before external manifestation of caisson disease. It was also established that bubbles first appear in the venae cavae, then in the aorta and pulmonary artery. As can be seen from a study conducted on dogs [5], the method of ultrasonic detection of gas bubbles permits demonstration of early stages of caisson disease and the opportunity to prevent severe forms of this disease when returning from a high ambient pressure. The authors report that with the development of appropriate sensors one can observe the process of appearance and growth of gas bubbles and, consequently, control submersion of divers and their return from deep waters. The possibility of detecting not only bubbles, but accumulations of erythrocytes, thrombocytes and fat cells, as factors related to the etiology of caisson disease, has been mentioned in several works [6, 7].

Our objective here was to test the possibility of using the ultrasonic method for detection of gas bubbles in the blood of different animals in a rarefied atmosphere.

Methods

We used an ultrasonic instrument made to our order by the Vil'nyus Scientific Research Institute of Radio Measuring Instruments to record gas bubbles in venous blood of animals. The operating principle of this instrument (Figure 1) is based on the Doppler effect. We used an ultrasonic frequency of 10 MHz. The cuff-type sensor consists of two barium titanate crystals soldered in plexiglas parallel to one another (Figure 2).

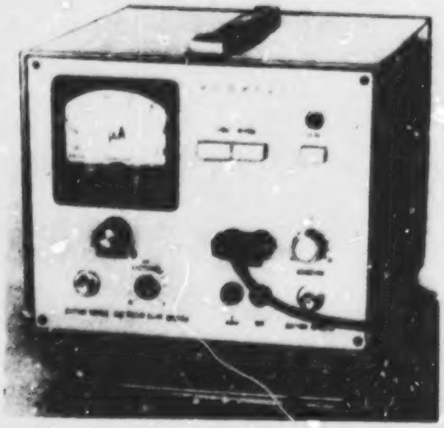

Figure 1.
Ultrasonic instrument

Figure 2. Ultrasonic sensors

In preliminary in vitro experiments, the sensor was connected to a polyvinyl chloride tube, through which we first passed tap water, then the same water but with bubbles injected with a syringe, and finally gassed water. The signals from the bubbles were heard through earphones and recorded on an electroencephalograph. In the in vivo experiments, anesthetized animals (rabbits and cats) were immobilized on a special table [stand]. We then exposed their abdominal cavity and secured the sensor on the surface of the posterior vena cava. The resulting Doppler signal was delivered to the electroencephalograph, with concurrent use of an oscillograph and telephone. The blood flow and respiration rate were recorded continuously during the entire experiment. The animals were "lifted" to "altitudes" of 12,000-14,000 m at the rate of 150 m/s in a Votsch-2 type oxygen chamber, where they remained for 40 min. After the experiment, the animals were dissected for a thorough examination of all blood vessels and the heart. In all, we conducted 45 experiments.

Results and Discussion

In the preliminary in vitro experiments with intravenous injection of air to rabbits we became convinced that the Doppler frequency signals change in amplitude and frequency upon appearance of gas bubbles in the liquid examined. When cats were "lifted" to an "altitude" of 12,000 m, we failed to demonstrate bubbles in any of the 10 experiments. They first appeared only at an "altitude" of 14,000 m, but bubbles were found in only 1 pregnant cat out of 14 experiments, in the 2d min at that "altitude" (Figure 3). As for rabbits, it was much easier for the gas-forming process to occur in them. Thus, in 5 cases out of 14 "ascents" to an "altitude" of 12,000 m, we demonstrated bubbles in venous blood of rabbits (Figure 4), whereas in the case of "climbs" to 14,000 m, gas bubbles were present in 4 cases out of 7. As a rule, the bubbles appeared in the first 20 min at the indicated "altitude." At the postmortem, bubbles were encountered in the femoral veins, subclavian veins of the abdominal wall, posterior vena cava and pulmonary vein.

Consequently, using the ultrasonic method we observed appearance of bubbles in animals in a significantly rarefied atmosphere. Our data are not in contradiction with the results of another study [8], where bubbles were visually demonstrable through an illuminator in the posterior vena cava at "altitudes" of at least 13,000 m. In our experiments, there was distinct demonstration of species-specific differences between animals, with

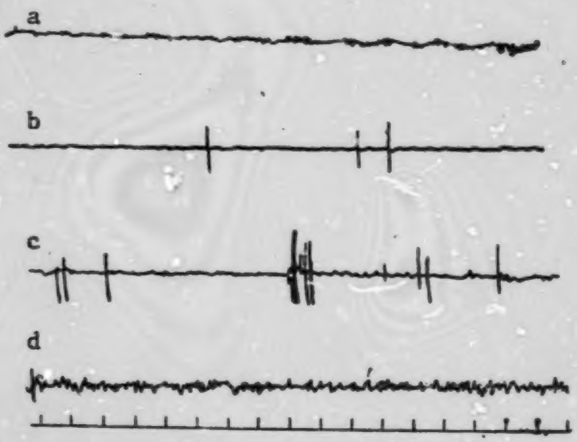

Figure 3.
Doppler signals from bubbles in a cat at an "altitude" of 13,000 m.
a) background blood flow
b) isolated Doppler signals in 2d min at 14,000 m
c) numerous signals from bubbles in the 5th min
d) absence of bubbles when animals returned to normal atmospheric pressure

respect to predisposition for gas production. In rabbits, bubbles appeared in venous blood with less rarefaction than in cats ($P<0.01$ and $P<0.02$ for "altitudes" of 12,000 and 14,000 m, respectively). We cannot rule out the possibility that differences in relative blood flow rate, physicochemical and morphological properties of blood have an influence on species-specific resistance to decompression disturbances.

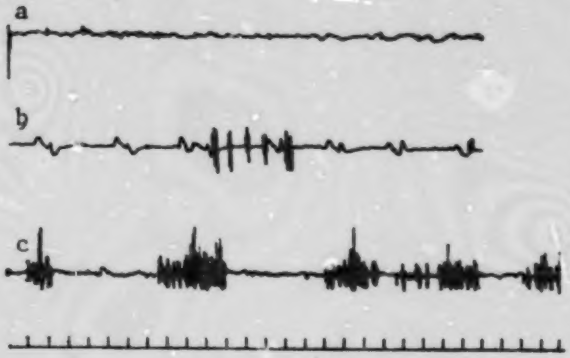

Figure 4.
Doppler signals from bubbles in rabbits at an "altitude" of 12,000 m

a) background blood flow
b) Doppler signal from bubbles in 4th min at this "altitude"
c) massive gas production; respiratory arrest

Thus, we have demonstrated the basic possibility of using the ultrasonic method to study the process of gas production in animals and man (with the use of special sensors) in a rarefied atmosphere. The feasibility of early detection of the moment of formation of gas bubbles in the body is very important in solving the problem of preventing decompression disorders. This method can be used in the system for monitoring the physiological condition of man at high altitudes.

BIBLIOGRAPHY

1. Smith, K., and Spencer, M. P. AEROSPACE MED., Vol 41, 1970, pp 1396-1400.

2. Gillis, M. F.; Karagianes, M. T.; and Peterson, P. U. SCIENCE, Vol 161, 1968, pp 579-580.

3. Powell, M. R. AEROSPACE MED., Vol 43, 1972, pp 168-172.

4. Rubissow, L. G., and Mackay, R. S. ULTRASONICS, Vol 2, 1971, pp 225-234.

5. Sapov, I. A.; Volkov, L. K.; Men'shikov, V. V.; et al. DOKL. AN SSSR [Reports of the USSR Academy of Sciences], Vol 222, No 2, 1975, pp 508-511.

6. Nishi, R., and Livingstone, S. D. AEROSPACE MED., Vol 44, 1973, pp 179-183.

7. Philp, R. B.; Inwood, M. J.; and Warren, B. A. Ibid, Vol 43, 1972, pp 946-953.

8. Harvay, E. B. "Animal Experiments on Bubble Formation. Pt 1. Bubble Formation in Cats. Decompression Sickness," Philadelphia, 1951, pp 115-144.

UDC: 543.544.25:613.693

ISOLATION AND GAS CHROMATOGRAPHIC DEMONSTRATION OF VOLATILE ORGANIC SUBSTANCES IN THIN-LAYER BIOLOGICAL SAMPLES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 77-79

[Article by N. F. Sopikov and A. I. Gorshunova, submitted 26 Jun 78]

[Text] In addition to chemical analytical methods, modern gas chromatographic methods are used to demonstrate organic compounds in studies of the effects of space flight factors and conditions (for example, hypokinesia, radiation, hypoxia, etc.) on processes of accumulation, distribution and elimination of volatile chemicals from the human and animal organism [1-6]. At the same time, the practical use of gas chromatography is related to a number of difficulties, due to the complexity, many stages and laboriousness of the process of isolating volatile chemicals from biological media and tissues [7-10].

Our objective was to develop a simple and rapid method for isolating volatile organic substances from biological media and tissues to be submitted to gas chromatographic analysis.

This method was based on the principle of direct thermal evaporation of volatile compounds from thin-layer biological samples, obtained by using a pyrolytic attachment with the chromatograph.

Volatile substances in blood and various animal tissues were demonstrated on a chromatograph with a flame-ionization detector. We selected the absorbent for the chromatographic column, its size and temperature in accordance with the composition and physicochemical properties of the volatile substances to be analyzed in biological samples. For example, for demonstration of 1,4-dioxane in blood and various animal tissues, we used a chromatography column 2.6 m in length and with an inside diameter of 3 mm filled with celite 545 [diatomaceous earth] (granulation 0.177-0.25 mm) with 15% polyethylene glycol 2000. The chromatographic column was incubated at a temperature of 75°C. Helium was used as the gas carrier. The flow rate for helium and hydrogen constituted 30 mℓ/min and air velocity was 300 mℓ/min. The temperature of the detector and unit for input of the gas sample was 150°C.

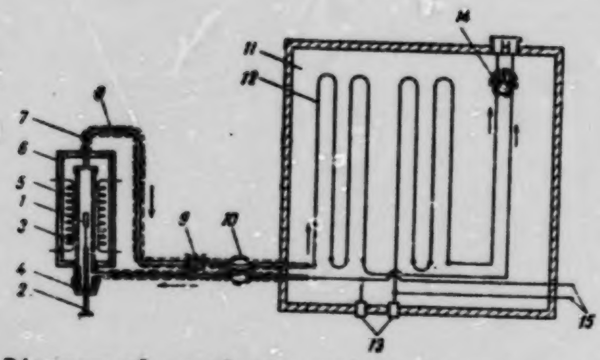

Figure 1. Diagram of pyrolytic attachment and gas lines of chromatograph

1) platinum boat
2) plunger
3) quartz tube
4) sealing coupling
5) electric heating coil
6) heater
7) connective capillary tube
8) heat-insulating sheath that is heated electrically
9) filter
10) four-way valve
11) thermostat chamber
12) chromatographic columns
13) unit for input of gas samples
14) detector
15) gas lines to tank with helium

Figure 1 illustrates the main units and system for connecting the gas lines of a tubular type attachment to the chromatograph.

In view of the high sensitivity of the flame-ionization detector of the chromatograph, we used milligram batches of biological samples. Blood, urine or organ tissue samples weighing 3 to 10 mg (usually 4-5 mg) were applied with an eye scalpel to pieces of tracing paper (10×4 mm^2, 2 mg) used as a backing, rapidly weighed on a type VT torsion balance accurate to 0.05 mg, then placed in the platinum boat *1* connected to plunger *2*, and immediately put in the unheated part of quartz tube *3*, which was sealed by turning coupling *4*, then the sample was moved with the sealed plunger into the region of the tube with a temperature of 120°C. All these operations required no more than 1 min, which reduced to a minimum any possible loss of analyzed substance due to evaporation during the process of preparing the biological sample for analysis. The use of a backing made of tracing paper ruled out direct contact between the biological sample and the boat of the pyrolytic attachment, and did not cause it to become contaminated.

We chose ordinary ["natural"] GOST 892-70 tracing paper as the most suitable material for the backing; it did not soften when wet, did not absorb substance and, at temperatures of up to 160°C, it did not discharge any impurities that would contaminate the sample. The use of such tracing paper did not affect the results of analysis, as confirmed by the same results from demonstration of standard aqueous solutions of the substances studied which were fed into the pyrolytic cell (on the backing and without it) directly in the platinum boat.

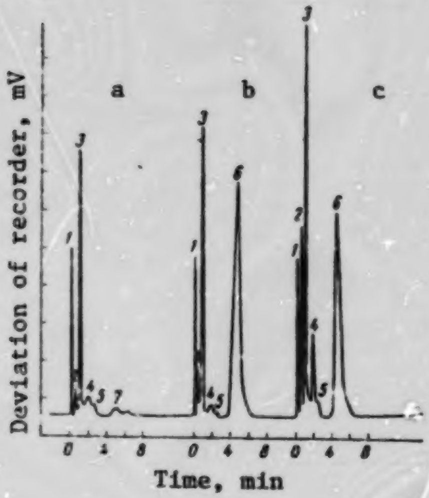

Figure 2.
Chromatogram of blood before giving dioxane (a), blood (b) and liver (c) after giving 250 mg/kg dioxane intraperitoneally
1) air
2) acetaldehyde
3) acetone
4,5) unidentified substances
6) dioxane
7) water

We found that it was sufficient to keep the biological sample in quartz tube *3* 5 mℓ in size for 2 min at 120°C to isolate organic compounds from it. Under such conditions, the sample was dehydrated, and there was denaturation of the tissue proteins it contained.

After exposure for 2 min, the discharged substances were fed through four-way valve *10* into the flow of gas carrier, through connecting capillary tube *7* and filter *9* to chromatographic column *12* for dilution, and then into the flame-ionization detector *14*.

In the gas chromatographic analysis, of biological samples, the discharged substances were recorded in the form of sharp and symmetrical peaks on the chromatogram. There was also a small and diffuse peak for water, which did not hinder detection of the analyzed substances and did not affect sensitivity of the detector (Figure 2). Concurrently, in addition to the peak for the compound administered, all chromatograms recorded the peaks for a number of endogenous substances that are formed during natural metabolism in tissues. The substances consistently demonstrable, which are released in significant quantities from different tissues, blood and urine, include, in particular, methane, ethanol, acetone, acetaldehyde and others, the concentrations of which reached 0.5-2.5 mg%.

We chose 1,4-dioxane, which has relatively low volatility (135 mg/ℓ), low rate of transformation and tissues and is well soluble in liquid biological media, to assess the accuracy of the analytical method.

In the experiments involving examination of blood, into which we first injected 1,4-dioxane in an estimated concentration of 0.2 μg/10 μℓ, we established that the results of gas chromatographic assay of dioxane in blood samples differed from assays of this substance in a standard aqueous solution, as well as from the estimated level, by only 2-5%, which was within the range of reading error. Repeated analysis of remainders of blood samples that previously contained 0.2 μg dioxane failed to demonstrate the latter, which was indicative of complete elimination thereof. Analogous findings were made in assaying dioxane content of tissues.

Rat brain and liver homogenates were prepared for quantitative assays of dioxane in tissues. Batches of tissues, each weighing 2.0 g, were put in 5-mℓ weighing bottles, into which we decanted different amounts of aqeueous dioxane solution containing 200 μg substance per mℓ, and mixed thoroughly. Concurrently, various amounts of standard dioxane solution were decanted into weighing bottles with 2.0 mℓ water. The results of analysis of 3-mg (4-5 mg) samples of tissue homogenates and water containing different concentrations of dioxane are listed in the Table.

Assays of dioxane in tissue homogenates and water (M±m)

Size of sample μg/g/mℓ	Dioxane demonstrated, μg/g		
	brain	liver	water
9,6	10,2±0,4	9,4±0,3	10,4±0,4
26,0	26,6±0,8	25,0±1,0	26,0±0,6
40,0	40,5±1,8	38,8±1,3	39,5±1,5
66,6	68,7±1,9	65,7±1,7	67,5±2,8
100,0	102,0±3,0	100,2±3,3	102,1±3,5

The data listed in this table indicate that there is good coincidence of results of analyzing dioxane in tissue homogenates and water. The error of assays, as compared to estimated levels, did not usually exceed 3-5%, and reached 11-12% in only a few cases with lower concentration of dioxane (9.6 μg/g).

It must be noted that the proposed method for analysis of organic substances permits assay thereof not only in homogenates requiring large tissue samples, but directly in thin-layer milligram samples. For this purpose, thin-layer sections were prepared from the liver of rats previously given dioxane, dichloroethane and other compounds; these sections were then placed on a backing of tracing paper, weighed and analyzed by the method described above. As a control, we assayed these substances in homogenates of tissue taken from the same region of the liver and applied to tracing paper in a thin layer. The difference between the results of analysis of sections and homogenates of the liver did not exceed 10%, which is within the range of error of the method.

Our data are indicative of the validity of using thin-layer sections instead of homogenates of tissues, and this has several advantages, particularly when studying the process of distribution of substances in the body. The simple and rapid preparation of biological samples reduces to a minimum any possible loss of volatile compounds. The small tissue samples (3-10 mg) permit examination of structures with low weight (adrenals, pituitary, etc.). It also permits, in particular, the study of distribution of chemicals in different parts of the central nervous system of small laboratory animals, such as mice and rats.

Thus, after intravenous injection of 1,2-dioxane in a dosage of 50 mg/kg, we demonstrated the following amounts (in mg%): 0.8 in the cerebral cortex, 0.93 in the thalamus, 0.66 in the hypothalamic region, 0.89 in the caudate nucleus, 0.6 in the hypophysis, 0.94 in the cerebellum, 1.2 in the lamina quadrigemina, 1.60 in the medulla oblongata and 2.65 in the spinal cord.

Thus, the proposed method is notably universal: it permits demonstration in the same biological sample of volatile organic substances, not only of exogenous, but endogenous origin; under identical (standard) conditions, it permits analysis of both liquid biological media (blood, urine) and various tissues and organs, which increases the reliability of results of comparative studies of distribution of chemicals in the body with exposure to various habitat factors.

The minimum demonstrable amounts of substances are in the range of 0.01 to 0.02 µg in the biological sample.

This simple and rapid micromethod for assaying volatile organic substances in biological media can be used in toxicological and hygienic studies for scientific diagnostic purposes in cases of acute and subacute poisoning.

BIBLIOGRAPHY

1. Bugar', K. P.; Kustov, V. V.; Abidin, V. I.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 6, 1977, pp 83-84.

2. Kustov, V. V.; Abidin, B. I.; Belkin, V. I.; et al. Ibid, No 1, 1976, pp 70-73.

3. Nefedov, Yu. G.; Zaloguyev, S. N.; and Savina, V. P. Ibid, No 2, pp 30-34.

4. Savina, V. P.; Sokolov, N. L.; and Nikitin, Ye. I. Ibid, No 6, pp 62-66.

5. Sokolov, N. L. "Studies of Composition of Microimpurities in Air Exhaled by Man and Their Role in Pollution of the Air Environment of Hermetically Sealed Rooms," author abstract of candidatorial dissertation, Moscow, 1972.

6. Tiunov, L. A.; Kolosova, T. S.; Lazurenko, D. T.; et al. KOSMICHESKAYA BIOL., No 1, 1976, pp 61-65.

7. Mikulin, S. G.; Kurchatov, G. V.; and Kofanov, V. I. in "Farmakologiya i toksikologiya" [Pharmacology and Toxicology], Kiev, Vyp 10, 1975, pp 162-164.

8. Murav'yeva, S. I.; Osipenko, N. I.; and Gubina, N. B. GIG. TRUDA [Industrial Hygiene], No 7, 1974, pp 31-34.

9. Yavorovskaya, S. F., and Gubina, N. B. GIG. I SAN. [Hygiene and Sanitation], No 12, 1971, pp 61-68.

10. Iffland, R., and Dotzauer, G. ARZNEIMITTLEFORSCH., Vol 17, 1967, p 918.

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A STAND FOR SIMULATION OF PHYSIOLOGICAL EFFECTS OF WEIGHTLESSNESS IN LABORATORY EXPERIMENTS ON RATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 79-80

[Article by Ye. A. Il'in and V. Ye. Novikov, submitted 26 Jan 79]

[Text] We were governed by the following requirements in developing the stand for simulation of physiological effects of weightlessness in laboratory experiments on rats: provide for increased blood supply to the head part of the trunk; reduce to a minimum the influence of such undesirable incidental factors as immobilization and restriction of movement; eliminate entirely the weight load on the hind limbs with partially reduced load on the front ones, that the animal could use to move about, independently take in feed and water.

The stand consists of a frame, on which a beam with movable carrier can move over two guide rails (see Figure). The carrier can move in any direction in the horizontal plane above wire flooring 40×40 cm in size, under which a tray is placed to collect excrements. A special system is used, which consists of a capron [nylon-6] rat suit with openings for the limbs and a wire frame, to suspend the animal on the carrier, in order to obtain uniform distribution of the weight load on the trunk.

The animal is suspended in such a manner as to totally eliminate any weight load on the hind legs by partially lifting the entire animal in a tilted position, the the head end down. Such suspension partially removes the weight load on the rat's forelegs and, in addition, creates conditions for increased supply of blood to the head end of the trunk. The animal can move about freely using its front legs over the wire flooring of the stand, in any direction, it can come up on its own to the feeder and water container, and use them. As shown by tests on this stand, retention of mobility has a favorable effect on the animal's general condition; it also eliminates restlessness and aggressiveness, which are inherent in the first days of experiments under hypokinetic conditions.

General view of stand; described in the text

Morey proposed an analogous principle for modeling the physiological effects of weightlessness in laboratory experiments on rats [1]. However, the design of the stand and, particularly, the suspension system differ from what we have described above. According to Morey, comparative analysis of the findings in rats that had spent the same length of time aboard Cosmos biosatellites and in suspended position on the stand revealed identical changes in bones of the limbs and rate of weight gain. All this means that the proposed method can be used with success for laboratory studies of mechanisms of some physiological reactions that occur in animals under weightless conditions.

BIBLIOGRAPHY

1. Morey, E. BIOSCIENCE, Vol 29, 1979, pp 168-172.

BRIEF REPORTS

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GLYCOPROTEIN CONTENT OF HUMAN BONE TISSUE AFTER SPACE FLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 81-82

[Article by A. A. Prokhonchukov and V. K. Leont'yev, submitted 10 Oct 78]

[Text] The state of calcium metabolism in the body during exposure to space flight factors and, chiefly, weightlessness is one of the pressing problems of space biology and medicine. In spite of the fact that some advances have been made in the study thereof, this problem remains unclear and debatable in many respects [1].

The main factor of dynamic stability of the mineral fraction of osseous tissue (chiefly calcium) is the close correlation between minerals and the organic fraction of osseous tissue, most of which consists of collagen and noncollagen proteins, and glucosamine glycans. Noncollagen proteins of mineralized tissues constitute a little-studied group of glycoproteins of connective tissue, the carbohydrate part of which is chemically bound with the protein part and consists of fucose, neuraminic acid, hexosamines and other sugars [2-5]. They are the most active proteins of connective tissue, as indicated by their involvement in fibril formation, aggregation of collagen fibers and their primary fixation of calcium [6-9]. Studies have shown that each type of mineralized tissue, in particular bone as an organ, is characterized by its own set of protein-bound carbohydrates. The glycoproteins determine the species-specific, functional and age-related distinctions of bone tissue. Glycoproteins play an important role in processes of formation and regeneration of collagen fibers [4, 8, 10]. There have been descriptions of impairment of their metabolism in the presence of bone pathology [4, 11].

Glucosamine glycans are involved in the transport and binding of fluid and inorganic ions in bone tissue [3, 4]. Changes in levels thereof have been demonstrated in experiments with hypokinetic rats [12].

Thus, glycoproteins and glucosamine glycans of osseous tissue are among the important elements of its homeostasis, related to the mineral and organic phases of bone, mechanism of fixation of calcium, most of which is contained in hydroxyapatite. Glycoproteins provide for the main mechanical qualities of bone, namely its plastic properties: resistance to flexing, torsion, stretching and compression loads.

Our objective included the study of glycoprotein content of the organic fraction of human bone tissue after a space flight (autopsy material from the crew of Salyut-1 orbital space station).

Methods

We used samples of osseous tissue from the calcaneus for our study [1]. This bone is subject to the main orthostatic and dynamic load, and it reacts sensitively to changes in gravity.

We used tissue from the calcaneus obtained from atuopsies on three men who died of acute trauma at the age of 20-40 years (without pathoanatomically demonstrable signs of diseases of viscera and systems) as a control for comparative analysis.

We treated the bones with proteolytic solution for complete removal of soft tissues [13]. Glycoprotein and glucosamine glycan content was assayed according to the quantity of protein-bound hexosamines, hexoses, fucoses, uronic and neuraminic acids and ketoses (in mg% dry bone weight, using the method described previously [14]). The digital data were submitted to statistical processing.

Results and Discussion

We demonstrated in all bone samples examined appreciable amounts of protein-bound carbohydrates: total hexoses, ketose, fucose, uronic and sialic acids, and hexosamines. This shows that, in addition to collagen protein, there were significant amounts of glycoproteins and glucosamine glycans in the bone tissue examined. The quantitative composition of glycoproteins of osseous tissue that we obtained coincides with data in the literature [2-4, 14, 15].

Comparative analysis of protein-bound carbohydrates in the test and control groups revealed that there was no statistically reliable difference in levels of most of the bone tissue components studied (see Table). We demonstrated a 23.5% decrease in uronic acid content and 19.5% increase in hexosamines of bone tissue in the tested group, as compared to the control; however, these differences were statistically unreliable (see Table). A comparison of our assays of glycoprotein content of bone tissue to data in the literature [2, 11, 14], including those related to diverse bone pathology [4, 14, 15], warrants the belief that the demonstrated changes in levels of different components of glycoproteins (uronic acids, ketoses) do not justify interpretation thereof as signs of bone pathology. Thus, we failed to demonstrate consistent deviations of composition of glycoproteins of human bone tissue after a space flight.

Glycoprotein content (mg%) of osseous tissue (M±m)

Glycoproteins	Group	
	control	test
Hexoses	1047,0±55,0	1013,0±27,0
Hexosamines	226,0±67,0	270,0±6,0
Sialic acids	26,3±2,4	23.7±1,4
Ketoses	65,0±12,0	67,0±4,0
Fucose	111,0±12,0	102,0±13,0
Uronic acids	213,0±34,0	163,0±32,0

On the basis of analysis of the literature and the results of these studies, it may be assumed that the findings confirm the previously expounded hypothesis, to the effect that the normal state of bone tissue after space flights is attributable to the high level of physical conditioning of cosmonauts and subsequent use, aboard the Salyut-1 orbital space station, of the set of equipment and conditioning measures to rule out the undesirable effects of space flight factors on the human body [1, 16, 17].

BIBLIOGRAPHY

1. Gazenko, O. G.; Prokhonchukov, A. A.; Panikarovskiy, V. V.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 3, 1977, pp 11-20.

2. Bourne, G. H. (editor) "The Biochemistry and Physiology of Bone," New York, Vol 1-3, 1971.

3. Vaughan, J. M. "The Physiology of Bone," Oxford, 1975.

4. Slutskiy, L. I. "Biochemistry of Normal and Pathologically Altered Connective Tissue," Leningrad, 1969.

5. Torbenko, V. P., and Kasavina, B. S. "Functional Biochemistry of Bone," Moscow, 1977.

6. Herring, J. M. BIOCHEM. J., Vol 159, 1976, pp 749-755.

7. Franzblan, C.; Schmidt, K.; Faris, B.; et al. BIOCHIM. BIOPHYS. ACTA, Vol 427, 1976, pp 302-314.

8. Leont'yev, V. K. in "Belki i fermenty v klinicheskikh i eksperimental'nykh issledovaniyakh" [Clinical and Experimental Studies of Proteins and Enzymes], Omsk, 1977, pp 44-46.

9. Leont'yev, V. K.; Desyatnichenko, K. S.; and Levchenko, L. T. Ibid, pp 46-49.

10. Kasavina, B. S., and Zenkevich, G. D. BIOKHIMIYA [Biochemistry], Vol 25, 1960, pp 669-672.

11. Casuceio, C. J. BONE JT. SURG., Vol 44B, 1962, pp 453-459.

12. Potapov, P. P. KOSMICHESKAYA BIOL., No 3, 1977, pp 44-48.

13. Gaydamak, A. N., and Leont'yev, V. K. in "Eksperimental'naya i klinicheskaya stomatologiya" [Experimental and Clinical Stomatology], Moscow, Vol 6, 1975, pp 46-49.

14. Leont'yev, V. K., and Gaydamak, A. N. LABOR. DELO [Laboratory Record], No 5, 1978, pp 290-293.

15. Prokhonchukov, A. A.; Zhizhina, N. A.; Leont'yev, V. K.; et al. in "Etiologiya i patogenez osnovnykh stomatologicheskikh zabolevaniy" [Etiology and Pathogenesis of the Main Stomatological Diseases], Moscow, 1977, pp 54-57.

16. Vasil'yev, P. V. in "Nevesomost'" [Weightlessness], Moscow, 1974, pp 278-297.

17. Stepantsov, V. I.; Yeremin, A. V.; and Tikhonov, M. A. Ibid, pp 298-313.

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VEGETOPOSTURAL REACTIONS IN ANTIORTHOSTATIC POSITION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 3, 1980 pp 82-84

[Article by K. L. Geykhman and M. R. Mogendovich, submitted 30 Oct 78]

[Text] Much significance is attributed to the antiorthostatic [head down] position (AOP) in simulating the physiological effects of weightlessness. This refers to the body's position in space that is opposite to orthostatic position.

Orthostasis is the usual state, which developed in phylogenesis and ontogenesis, and AOP elicits an extreme and biologically unstable state. It is not inherent in man, and it is often on the borderline of pathology.

Let us first discuss complete AOP (CAOP), i.e., vertical position with the head down. We tested the cardiovascular system, external respiration, motility in the initial (orthostatic) position, then during 1-min AOP and in the aftereffect period (return to orthostatic position). We had the following objectives: to determine how human physiological functions change; to trace the compensatory mechanisms of the body to normalize circulation in this position (homeostasis); to determine whether it is possible for these mechanisms to adjust by means of conditioning. We studied the changes in the autonomic nervous system by means of arterial oscillography, electrocardiography, pulsotachometry, cutaneous thermometry and oxyhemography. Concurrently, we measured the tonus of skeletal muscles with an electromyotonometer, and determined the latency period of motor reactions of the arms and legs to an exogenous signal [1, 2].

Our results revealed that the change from orthostatic position to CAOP is associated with drastic changes in activity of the cardiovascular system, oxygenation of blood and motility. CAOP is characterized by the following physiological changes: slowing of heart rate by a mean of 7.8/min in passive CAOP and by 2.3 in active CAOP' elevation of maximum and drop of diastolic pressure, elevation of oscillatory index and minor change in mean pressure in passive AOP; elevation of temperature of the skin on the forehead by 0.7°C in active position and 0.3°C in passive; 7.6% decrease in blood oxygenation. The changes in the autonomic nervous system were associated with drastic increase in tonus of arm muscles, some tonic tension of the legs in the active position, as well as longer latency period of the motor reactions of arms and legs.

Studies of athletes involved in different sports revealed that regular practice of special physical exercises improves reflex mechanisms that counteract gravity. The body adjusts to unusual positions, as a result of which there is attenuation of disturbances of the autonomic nervous system [3].

A set of adaptational and compensatory neurohumoral mechanisms are involved in normalization of the gravitational changes in blood in CAOP. Of basic importance is determination of the mechanism of postural and vegetative reflexes, which regulates the functional state of the cardiovascular system in CAOP by means of proprioceptive impulsation.

We studied postural and vegetative reflexes not only in CAOP, but with small angles of inclination, produced by using a special turntable or chair.

Data pertaining to passive AOP with a tilt angle of 30° were submitted in the work by G. Z. Chuvayeva [4, 5]. M. D. Berg reported the hemodynamic parameters of school children 7-8 and 14-16 years of age in the same position [6, 7]. V. A. Shchurov used passive AOP at an angle of 30° [8] and S. N. Khmeleva used angles of 30 and 45° [9]. Their findings confirm the existence of a correlation between postural tonus of skeletal muscles and condition of vessels (motor-vascular reflex).

Later on, R. M. Bayevskiy used AOP with 15 and 30° angles [10]. Studies involving the use of long-term hypokinesia [11, 12] revealed that AOP with a tilt angle of -4° is more demonstrative than the horizontal position. AOP with angles of -4, -8, -12, -16 and -20° was used by other authors also [13-15]. At the suggestion of M. R. Mogendovich, in addition to ordinary AOP (with the legs straight), a special AOP with the legs elevated and bent at the knees was used. This position was named "position No 2." This position is a more effective model of redistribution of blood in weightlessness than position No 1 [15-19]. Underestimation of the leg position in AOP could lead to misinterpretation of minute volume and other hemodynamic parameters. A combination of AOP and prolonged hypokinesia yields particularly rich information.

Further studies are needed for use of data obtained in tests with AOP in screening cosmonauts and developing preventive measures [20].

BIBLIOGRAPHY

1. Geykhman, K. L. "The Most Important Vegetative Changes in Man in Antiorthostatic Position," candidatorial dissertation, Perm', 1965.

2. Geykhman, K. L., and Zuyev, R. V. in "Nauchno-prakticheskaya konf. po fizicheskomy vospitaniyu, fiziologii sporta, vrachebnomu kontrolyu i lechebnoy fizicheskoy kul'ture. 2-ya. Materialy" [Proceedings of 2d Scientific and Practical Conference on Physical Education, Physiology of Sprots, Medical Monitoring and Therapeutic Physical Culture], Perm', 1967, pp 64-66.

3. Alekseyev, D. A.; Yarullin, Kh. Kh.; Krupina, T. N.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1974, pp 66-72.

4. Chuvayeva, G. Z. in "Motorno-vistseral'nyye i pozno-vegetativnyye refleksy" [Visceromotor and Vegetopostural Reflexes], Perm', 1965, pp 54-58.

5. Chuvayeva, G. Z. in "Novoye v fiziologii i patologii motorno-vistseral'nykh refleksov" [News in Physiology and Pathology of Visceromotor Reflexes], Perm', 1967, pp 42-46.

6. Berg, M. D. in "Motorno-vistseral'nyye i pozno-vegetativnyye refleksy," Perm', 1965, pp 59-65.

7. Berg, M. D. "Age-Related Aspect of Vegetopostural Reflexes of the Cardiovascular System," candidatorial dissertation, Perm', 1967.

8. Shchurov, V. A. "Functional Studies of Age-Related Distinctions in Delivery of Blood to the Human Limbs," candidatorial dissertation, Perm', 1969.

9. Khmeleva, S. N. in "Voprosy fizicheskoy kul'tury i sovershenstvovaniye uchebnogo protsessa" [Problems of Physical Culture and Refinement of the Learning Process], Volgograd, Vyp 1, 1969, pp 245-247.

10. Bayevskiy, R. M. FIZIOL. ZH. SSSR [Physiological Journal of the USSR], No 6, 1972, pp 819-827.

11. Genin, A. M., and Kakurin, L. I. KOSMICHESKAYA BIOL., No 4, 1972, pp 26-28.

12. Pometov, Yu. D., and Katkovskiy, B. S. Ibid, pp 39-46.

13. Sidorov, N. I. in "Teoriya i praktika fizicheskogo vospitaniya i sporta" [Theory and Practice of Physical Education and Sports], Perm', 1975, pp 141-142.

14. Gubman, L. B. Ibid, pp 89-90.

15. Gubman, L. B.; Komin, S. V.; and Petrov, B. V. in "Vozrastnyye osobennosti dvigatel'nykh i vegetativnykh funktsiy i ikh vzaimodeystviye pri razlichnykh vidakh myshechnoy aktivnosti" [Age-Related Distinctions of Motor and Autonomic Functions, and Interaction Thereof During Different Forms of Muscular Activity], Kalinin, 1973, pp 123-134.

16. Geykhman, K. L.; Gusev, A. N.; Degtyarev, P. G.; et al. in "Aviakosmicheskaya meditsina" [Aerospace Medicine], Moscow—Kaluga, Vol 2, 1975, pp 127-130.

17. Gubman, L. B., and Petrov, B. V. in "Nauchnyye osnovy fizicheskoy kul'tury" [Scientific Bases of Physical Culture], Kalinin, Vyp 2, 1974, pp 12-28.

18. Degtyarev, P. G., and Mogendovich, M. R. in "Vozrastnyye osobennosti motorno-vistseral'noy regulyatsii pri razlichnykh vidakh myshechnoy activnosti" [Age-Related Distinctions of Visceromotor Regulation During Different Types of Muscular Activity], Kalinin, Vyp 3, 1975, pp 65-66.

19. Petrov, B. V. Ibid, pp 67-76.

20. Geykhman, K. L., and Mogendovich, M. R. KOSMICHESKAYA BIOL., No 3, 1977, pp 74-75.

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USE OF CYTOCHEMICAL PARAMETERS OF PERIPHERAL BLOOD NEUTROPHILS TO STUDY HORMONAL AND ENDOCRINE REACTIONS TO FLIGHT WORK LOADS

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[Article by P. S. Pashchenko, A. V. Pastushenkov, V. V. Grishchenko and I. V. Lemak, submitted 4 May 79]

[Text] Since pilot work is related to constant emotional stress, some investigators [1-4] used methods that enabled them to study the reaction of the adrenohypophyseal system to the complex effects of flight factors: 17-hydroxycorticosteroid (17-HCC) content of urine, precipitation color reaction according to Kimbarovskiy (PCRK) and others. Elevation of corticosteroid, sugar, choleterol levels in blood, as well as 17-HCC in urine of pilots, after completing flights were usually related by authors to high levels of nervous and emotional tension. Analysis of data obtained for PCRK is difficult because of the low specificity of this reaction and its unclear chemistry [5].

Our objective was to find an adequate object and certain indicators of humoral and endocrine influences in pilots as related to different levels of flight work.

In our opinion, one should use cells of tissues that are not subject to direct neural regulation (i.e., that do not contain nerve cells), in which regulatory processes are implemented by incretory influences, as the object of investigation to isolate the hormonal-endocrine component of the general system of regulatory influences. The cellular elements of peripheral blood are adequate and accessible objects of this type. For these cells, the exogenous environment is blood plasma, in which a chain of hormonal effects develops, which induce various chemical conversions in the cells.

Flight work activates the pilot's adrenohypophyseal system, and this is associated with elevation of blood catecholamines and urine 17-HCC [1, 4], leading to a change in carbohydrate metabolism. The effect of catecholamines on carbohydrate metabolism of cells can also be studied indirectly. It is known that glycogen breaks down in cells as a result of increase in phosphorylase activity. This enzyme changes from inactive to active form as a result of the mediated effect on it of such incretory substances as epinephrine and glucagon (there are data to the effect that their influence on carbohydrate metabolism is similar to some extent [6]. In our studies, glycogen content of neutrophil cytoplasm and activity of phosphorylase in neutrophils served as indicators of the regulatory influence of adrenalin on carbohydrate metabolism of cells.

Methods

We took blood from the finger. The PAS reaction according to McManus and Hotchkiss was run to demonstrate cytochemically cytoplasmic neutrophils. This substance was identified in control blood smears by treating them with a saliva solution for 30 min at a temperature of 37°C. Phosphorylase was demonstrated by the method of Tekeuchi [7]. We assessed glycogen content of cells on the basis of optical density of the reaction product, using the method of single-beam scanning cytophotometry with a cytophotometer designed on the order of the MUF-6 type (photographic variant) in the laboratory of histological chemistry of Voronezh Medical Institute. Optical density of the product of the cytochemical reaction was calculated with the following formula:

$$\varepsilon = \frac{1}{\log I_1 - \log I_2}$$

where ε is optical density, $\log I_1 - \log I_2$ is the logarithmic difference characterizing attenuation of the optical beam. The error factor of the method is in the range of 10% [8].

We assessed cytochemical activity of phosphorylase according to number of granules in the product of the cytochemical reaction, on the basis of the fact that the number of granules of this enzyme reflects the number of its "active centers" in cell cytoplasm. We studied 30 cells for demonstration of the substances in question in each pilot (student) under experimental conditions and in the background. The data were submitted to statistical processing with the use of Student's criterion.

We examined 10 students after 2 introductory flights and 8 pilots after 3 test flights 1.5-2 h before the flights (background) and 10-15 min after the flight shift was over (experiment). The flight work load was assumed to be insignificant for the students, unlike pilots, since they did not participate directly in piloting the aircraft (which was controlled by experienced instructors).

Results and Discussion

After two introductory flights, glycogen content of blood neutrophils did not differ reliably (P>0.05) from the levels demonstrated 1.5-2 h before the flights. Phosphorylase activity was also virtually the same as in the background (see Table). Thus, there is no reason to believe that humoral and endocrine reactions had any marked influence on carbohydrate metabolism of peripheral blood cells after the students' two introductory flights.

Some cytochemical parameters of carbohydrate metabolism of peripheral blood neutrophils of pilots and students after completion of flights for different purposes

Cytochemical parameter	Flight load	Time of study	
		1.5-2 h before flight	10-15 min after flight shift
Optical density of product of cytochemical reaction for glycogen in neutrophil cytoplasm, arbitrary units (M±σ)	Two introductory flights (students)	22.3±8.7	20±9.0
Mean number of granules of product of cytochemical reaction for phosphorylase in neutrophil cytoplasm		8.8±3.9	9.5±2.7
Optical density of product of cytochemical reaction for glycogen in neutrophil cytoplasm, arbitrary units (M±σ)	Three pilotage flights (pilots)	36.0±13.7	22.5±10.1*
Mean number of granules of product of cytochemical reaction for phosphorylase in neutrophil cytoplasm		9.8±2.4	15.6±3.8

*$P<0.05$

The findings were different with regard to glycogen content and phosphorylase activity. After the flight shift (see Table), there was a reliable decrease in glycogen content of neutrophil cytoplasm (by 39%) and increase in phosphorylase activity in the pilots. This is indicative of obvious intensification of endocrine influence on blood cell chemistry, and according to current conceptions this shows intensification of incretory function of the adrenal cortex [9].

This conclusion is consistent, to some extent, to the data of other authors, who observed an increase in 17-HCC in urine after flights [3].

We became convinced that the glycogen outlay was unrelated to performance of a specific function by neutrophils by the fact that we failed to demonstrate phagocytosis in these cells, since we took material for our study from essentially healthy individuals.

Thus, the parameters of carbohydrate metabolism of blood neutrophils that we studied can serve as a sort of "mirror" of hormonal and endocrine reactions to flying work loads.

BIBLIOGRAPHY

1. Arutyunov, G. A.; Vorob'yev, N. A.; Kuznetsov, N. I.; et al. VOYEN.-MED. ZH. [Military Medical Journal], No 1, 1963, pp 60-64.

2. Dlusskaya, I. G.; Kosmolinskiy, F. P.; and Fedorov, N. A. in "Aviatsionnaya i kosmicheskaya meditsina" [Aviation and Space Medicine], Moscow, 1963, pp 165-169.

3. Kosmolinskiy, F. P. VOYEN.-MED. ZH., No 6, 1965, pp 63-64.

4. Idem, "Emotional Stress When Working Under Extreme Conditions," Moscow, 1976.

5. Bokunyayeva, N. I. in "Spravochnik po klinicheskim laboratornym metodam issledovaniya" [Manual of Clinical Laboratory Test Methods], Moscow, 2d edition, 1975, pp 232-233.

6. Sutherland (1956, 1959) quoted in "Vvedeniye v klinicheskuyu biokhimiyu" [Introduction Into Clinical Biochemistry], edited by I. I. Ivanov, Leningrad, 1969, p 430.

7. Lilly, R. "Pathohistological Techniques and Practical Histochemistry," edited by V. V. Portugalov, Moscow, 1969, pp 306-307.

8. Pevzner, L. Z. "Functional Biochemistry of Neuroglia," Leningrad, 1972, pp 32-33.

9. Ivanov, I. I.; Zarembskiy, R. A.; Korovkin, B. F.; et al. "Vvedeniye v klinicheskuyu biokhimiyu," Leningrad, 1969.

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EVALUATION OF THE FUNCTIONAL STATE OF THE HUMAN CARDIOVASCULAR SYSTEM DURING PROLONGED ANTIORTHOSTATIC HYPOKINESIA, USING DIFFERENT LEVELS OF PHYSICAL EXERCISE ON A BICYCLE ERGOMETER

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No 3, 1980 pp 86-87

[Article by B. S. Katkovskiy and V. P. Buzulina, submitted 3 Feb 78]

[Text] The functional tests involving physical loads of about 400 kg-m/min during the flight aboard Salyut-4 orbital station failed to demonstrate appreciable changes in functional state of crew members [1]. At the same time, signs indicative of poorer endurance of physical work were found in all of the cosmonauts after the flights [2]. The discrepancies between flight and postflight data could be due to the fact that the postflight tests were conducted during the acute period of readjustment to earth's gravity, as well as that the test load was somewhat greater (600 kg-m/min) in the preflight and postflight tests than during the flight.

The reaction of the human body to physical work is determined by the extent and duration of such work. It is a known fact that the values of different parameters of the circulatory system at rest (particularly when one fails to adhere to the usual conditions for testing basal metabolism) may vary from test to test over a rather wide range in the same person. Emotional and other influences are not entirely eliminated with small physical work loads, and therefore the results of functional tests with a small load could also vary, thus making it difficult to demonstrate the influence of the factor under study. One generally simulates the influence of weightlessness on the cardiovascular system in the laboratory by means of ordinary bed rest or hypokinesia in antiorthostatic (ANOH) position [head tilted down] [3-5]. Unquestionably, physical exercise performed "lying down" is a more adequate model of the functional tests that the cosmonauts perform during a flight than the same exercise performed in "seated" position. For this reason, we planned to conduct tests with different levels of physical loads with the subjects in "lying down" position in the study involving prolonged ANOH (-4°).

Methods

We conducted the studies on 12 volunteer subjects who had undergon special medical screening and were deemed to be essentially healthy. After the background studies, the subjects were divided into two groups, with six people in each. We used anthropometric data, as well as indices of resistance to various (including maximum) physical loads and orthostatic tests, in order to form homogeneous groups. The first group of subjects performed a set of physical exercises developed and tested by V. A. Tishler [6], twice a day while in ANOH. The caloric value of the exercises constituted about 300 kcal/h. The second group (control) did not exercise. Before and on the 45th day of ANOH, all of the subjects performed 5-min tests with physical loads of 150, 300, 600 and 800 kg-m/min in "lying down" position. There was a 5-min interval between the first and second load, and 10-15-min between subsequent ones.

Results and Discussion

We analyzed the pulse rate recorded in the 5th min of each physical load. Our findings and data in the literature indicate that, in most cases, this is enough time for various parameters of the cardiovascular and respiratory systems to establish a " table state" [7]. As can be seen in the Table, there were insignificant intergroup differences in the background period with the different physical loads.

Pulse rate in the 5th min of tests with graduated physical loads performed "lying down" before (background) and on the 45th day of ANOH

Group	Subjects	Load (kg-m/min) and time of test											
		150			300			600			800		
		BG	45th day	Δ	BG	45th day	Δ	BG	45th day	Δ	BG	45th day	Δ
1	D-ov	101	106	+5	105	110	+5	119	123	+4	134	131	−3
	A-yev	87	91	+4	94	99	+5	110	117	+7	131	130	−1
	M-ov	83	80	−3	95	88	−7	114	108	−6	132	127	−5
	P-ov	75	83	+8	85	90	+5	100	106	+6	110	114	+4
	G-ov	92	92	0	98	95	−3	124	125	+1	129	160	+31
	G-in	99	95	−4	109	108	−1	133	134	+1	150	157	+7
2	A-ov	93	115	+22	99	125	+26	126	165	+39	154	173	+19
	P-ov	90	88	−2	98	105	+7	112	126	+14	114	141	+27
	K-ov	82	83	+1	89	95	+6	116	125	+9	128	149	+21
	F-ov	121	115	−6	123	125	+2	145	157	+12	159	174	+15
	O-ov	92	88	−4	97	100	+3	120	128	+8	140	164	+24
	Sh-ov	86	77	−9	92	83	−11	106	103	−3	112	130	+18

Note: Δ refers to difference between pulse rate on 45th day of ANOH and in the background period; BG--background.

In most subjects who worked out, the pulse reaction to physical loads only changed insignificantly under the influence of ANOH. Changes occurred in different directions, not only from person to person, but in the same subject from load to load. In only 1 case did the pulse rate increase by 31/min with a load of 800 kg-m/min. The same subject demonstrated other signs of deterioration of the functional state of the cardiovascular system: extrasystoles after loads of 600 and 800 kg-m/min.

The subjects in the second group presented substantially decreased endurance of physical exercise; however, this was distinctly demonstrable with relatively heavy physical loads. Thus, the mean group reaction of pulse rate to a load of 150 kg-m/min showed virtually no change, as compared to the background, and increased negligibly with a load of 300 kg-m/min (see Table). With a load of 800 kg-m/min, all 6 subjects showed an increase of 15-25/min in pulse rate, as compared to the background load. In 1 case, the test was stopped at the subject's request because he did not feel well. With a load of 600 kg-m/min, an increased pulse reaction was demonstrated in 5 out of the 6 subjects.

Thus, our data indicate that small physical loads are not demonstrative for evaluation of functional changes in the human cardiovascular system in studies simulating prolonged weightlessness. Evidently, even in a real space flight, the functional state of crew members should be assessed with the use of physical loads of at least 800 kg-m/min, particularly when the flight program requires significant physical exertion of the cosmonaut.

BIBLIOGRAPHY

1. Vorob'yev, Ye. I.; Gazenko, O. G.; Gurovskiy, N. N.; et al. KOSMICHESKAYA BIOL. [Space Biology], No 5, 1976, pp 3-18.
2. Beregovkin, A. V.; Vodolazov, A. S.; Georgiyevskiy, V. S.; et al. Ibid, pp 24-30.
3. Genin, A. M., and Kakurin, L. I. Ibid, No 4, 1972, pp 26-28.
4. Parin, V. V., and Krupina, T. N. in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii" [Adjustment to Muscular Activity and Hypokinesia], Novosibirsk, 1970, pp 134-135.
5. Kakurin, L. I., and Katkovskiy, B. S. in "Fiziologiya cheloveka i zhivotnykh" [Human and Animal Physiology], Moscow, 1966, pp 6-29.
6. Kakurin, L. I.; Katkovskiy, B. S.; Timler, V. A.; et al. KOSMICHESKAYA BIOL., No 3, 1978, pp 20-27.
7. Katkovskiy, B. S. "Some Distinctions of Oxygen Uptake During Physical Exercise After Long-Term Restriction of Man's Motor Activity," candidatorial dissertation, Moscow, 1966.

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